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VOLUME 84 May, 1947 NUMBER 5

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VOLUME 84 MAY, 1947 NUMBER 5

TREATMENT OF TRICHOMONAS VAGINALIS VAGINITIS

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MITCHELL J. NECHTOW, M.D., Chicago, Illinois

THE treatment of Trichomonas vaginalis vaginitis was approached, for the investigation here reported, as a problem involving: (1) the effectiveness of the therapeutic agent under test, and (2) the effectiveness of the steps taken against recurrence.

The work was done in the outpatient gynecological clinic at Cook County Hospital, Chicago, and in the private practice of the investigators participating; 2080 patients were examined for presence of Trichomonas vaginalis infection; 541 were found to be positive; 205 were available for study; and 153 were followed with sufficient completeness for report.

PROCEDURE AND RESULTS

Differential diagnosis and examination. A history was taken and a preliminary examination made of the vulva, with particular attention to the character, amount, color, and odor of the discharge.

Irritation and itching usually were complained of, in association with a leucorrhea and pruritis; bladder indications of frequency and urgency often were present; and, occasionally, dyspareunia, vaginospasm, and sensation of heaviness.

Examination of the vulva revealed skin manifestations of infection, ranging from normal skin to extensive vulvitis (Figs. 1 and 2 insert). Perirectal irritations and, occasionally, accompanying condylomata acuminata were found. The common finding was that of an inflamed mucous membrane, with pinpoint petechiae dispersed over the cervix. Examination of Skene's glands and the openings of the Bartholin glands showed evidence of infection in more than 50 per cent of the strongly positive trichomonas cases. Cervicitis, endocervicitis with erosions, polyps, and nabothian cysts frequently were found as incidental pathology. Tender, indurated sacrouterine ligaments were found in approximately 5 per cent of the apparently acute, strongly positive cases.

Unlubricated speculums were used for the vaginal examination. After noting all pathology, *p*H determinations were made with nitrazine paper. Next, the type of vaginitis was identified through microscopic examination of a hanging drop of vaginal secretion and, frequently, an undiluted wet smear and Gram stain.

The specimen for microscopic examination was prepared by releasing, onto a drop of normal saline on the cover slip, a drop of secretion obtained from the posterior fornix by means of an 8 inch glass tube tapered at the "sampling" end and with a rubber bulb to provide suction at the other.

The number of trichomonads was counted under high power magnification. A field containing only an occasional trichomonad, or less than 3, was classified as +. A field con-

From the Gynecological Division of the Fantus Clinics, the Cook County Graduate School of Medicine and the Hektoen Institute for Medical Research, Cook County Hospital.

taining 3 to 8 was classified as ++ and one containing more than 8 as +++ or ++++.

When the urethra and bladder were suspected as foci, particularly after patients who had been given extensive treatment presented themselves again for treatment, a hanging drop examination was made on a catheterized specimen of residual urine taken from the bladder before removal of the catheter (for avoidance of contamination from the urethra).

Initial treatment. Each patient that presented herself for treatment, after being found to be trichomonas-positive, was placed on a strict clinic-home regimen. A course of treatment was begun, directed not only toward the elimination of the vaginal trichomonads but also to those foci and existing pathological conditions that could contribute as complications in prolonging the infection.

In those cases in which there was a focus or foci of Trichomonas vaginalis infection within the internal and external genitalia, treatment was instituted as follows:

a. Electrofulguration of Skene's ducts (numbering from 2 to 11 as noted by one of us, H. L. B.),
b. Electrocautery of cervical erosions (first degree);
c. Electrocoagulation of cervical erosions and nabothian cysts and of the endocervix in endocervicitis including bilateral transverse lacerations allowing "pocket formation";
d. Removal of cervical polyps; and
e. Electrocoagulation of eroded ectropion of either anterior or posterior cervix.

The procedure for elimination of the vaginal trichomonads consisted of drying the vaginal tract and then applying, by insufflation (Figs. 3 and 4), from 2 to 4 grams of a powder containing 20 per cent by weight of finely pulverized argyrol, 40 per cent of kaolin, and 40 per cent of beta-lactose.

In the severe, acute cases in which there was pronounced tenderness in the vagina, the preliminary drying was omitted and the discharge simply wiped away before insufflation.

The insufflation was given with a Graves speculum in place,[1] producing distention of the vaginal walls and allowing deposition of the powder in the anterior and posterior fornices. As the speculum was withdrawn, insufflation was carried backward toward the vulva.

A sanitary napkin was provided. The patient was then instructed to take a douche nightly, containing white vinegar (4 tablespoonfuls to 2 quarts of warm water) followed by insertion high into the vaginal tract of a No. 12 gelatin capsule containing an additional 4 grams of the argyrol, kaolin, and lactose powder. A supply of 6 of these capsules was given—the requirement for 1 week—and the patient asked to return for re-examination at the end of one week from the day of clinic treatment, after having taken the douche only (and no capsule) on the night preceding re-examination. The patient also was instructed to give careful attention to the following prophylactic measures:

1. Wipe backward with toilet paper, using separate piece for the urethra.
2. Wash hands after bowel movement and also before insertion of vaginal wick used during menstruation.
3. Wash external parts with soap and water (between the labia and about the clitoris and introitus) before douching; boil douche-tip and run hot water through douche bag for 3 minutes before using.
4. Avoid use of saliva for lubrication during intercourse; douche before and after intercourse, if still under treatment, followed by insertion of a capsule.
5. Use an absolutely clean bathtub.

Contamination from the rectum and mouth is stated by Bland and Rakoff to be "rarely, if ever, a source of vaginal infestation," but should not be permitted to occur. Bed-pan contamination also must be guarded against. Especial care must be taken, where others use the same douche bag and tip and bath-tub, to prevent the infection being spread to them. Prophylactic use of a mild antiseptic douche, preferably an oxychlorine preparation, immediately following exposure to a likely con-

[1] It is suggested that a speculum always be used for insufflation. An insufflator should never be applied so that the rubber diaphragm fits snugly against the vulva while an insufflation is being given, because of the possible danger of producing an air embolism. In the pregnant patients, vaginal powder applications by means of insufflation must be made with speculum in place and the vagina well distended, a minimum of pressure being used, and with the insufflator tip directed into the fornices and well away from the cervix.

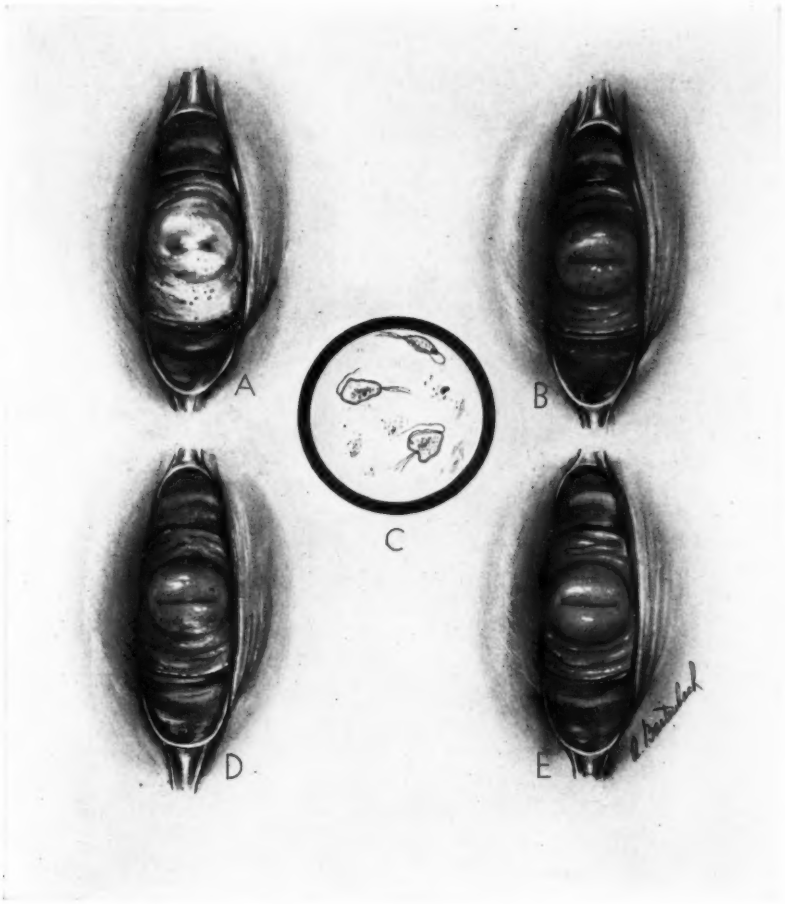

Fig. 1. Clinical appearance of Trichomonas vaginalis vaginitis and the results of treatment. A, Typical picture; B, discharge wiped away exposing petechial spots on the cervix caused by the Trichomonas vaginalis; C, microscopic view of Trichomonas vaginalis under high power; D, clinical appearance of vagina after 1 week of therapy; E, clinical appearance of vagina after eradication of infection.

Treatment of Trichomonas Vaginalis Vaginitis —
Walter J. Reich, Helen L. Sutton, and Mitchell J. Nechtow

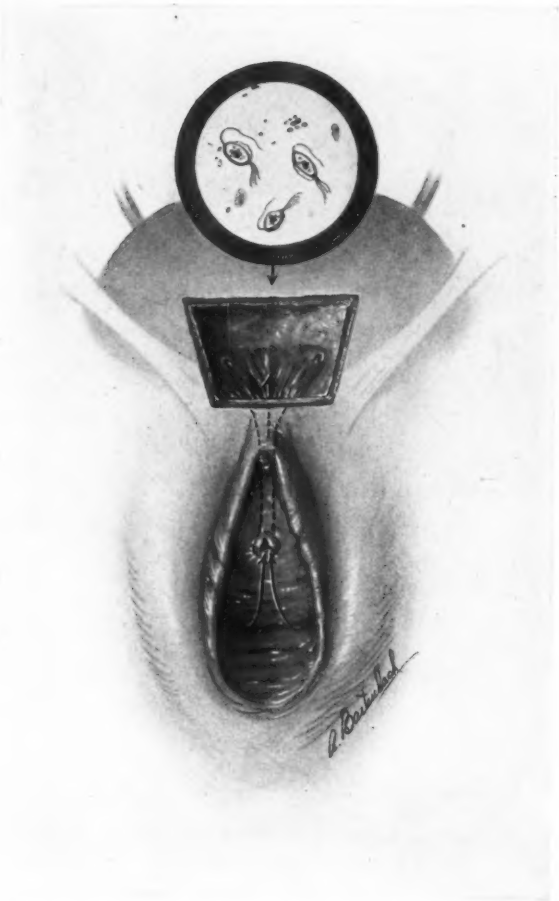

Fig. 2. Contiguous trigonitis due to Trichomonas vaginalis vaginitis.

Treatment of Trichomonas Vaginalis Vaginitis.—
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taminated tub, pool, toilet seat, linens, or sexual congress may provide a reasonably safe means of protection.

The possibility of the male as a source of infection has been forcefully emphasized by Feo (4) who states that "the male is not only responsible for the reinfection of women but is the principal agent of transmission." Allison terms trichomoniasis the "seventh venereal disease." Proper feminine hygiene measures should be taken, particularly where reinfection is suspected and later proved to have come from the marital partner.[1]

Safety. The instruction to return for re-examination at the end of each consecutive week of treatment permitted close observation of progress and also, at the beginning of the study, the very necessary assurance that the treatment was altogether safe for continued use. No indication of harmful effect was found at any time and no instance of sensitivity to type or method of treatment. No argyria was seen. (Long continued use of any silver preparation carries with it a risk of argyria and should be avoided. A search through the published records up to 1939, by Hill and Pillsbury, found record of no

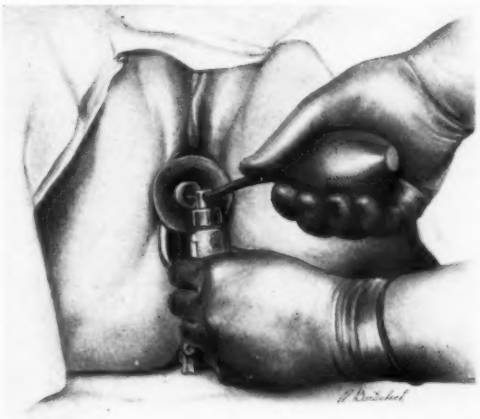

Fig. 3. Insufflation of argyrol compound powder, front view.

Fig. 4. Insufflation of argyrol compound powder, lateral view.

[1]Dr. J. Lester Wilkey of the Genito-Urinary Department of Cook County Hospital, Chicago, has observed (private communication) in 13 of a series of 16 instances of Trichomonas vaginalis infection in the male, the presence of urethral strictures derived from an earlier gonorrheal infection, and suggests that such strictures may act as dams behind which trichomonads may be harbored. The treatment given consisted of prostatic massage with urethral dilatation once weekly followed by anterior-posterior instillation of a 5 per cent solution of mild silver protein, with precaution against reinfection. A 5 per cent solution of mild silver protein was prescribed for interim urethral injection by the patient twice daily.

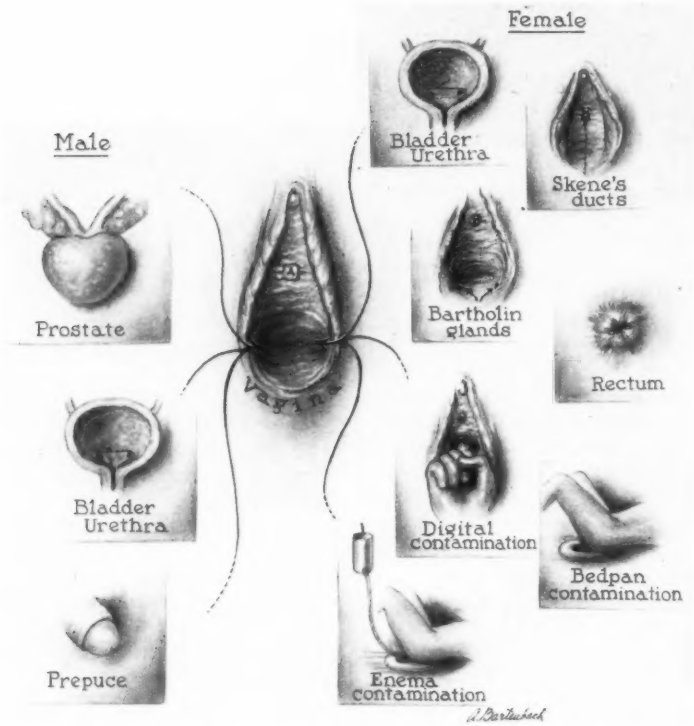

Fig. 5. Composite drawing showing possible sources of reinfection.

instance of generalized argyria associated with the use of mild silver protein as the only form of silver given, in the genitourinary region, but did find report of one instance following a combined use of mild and strong silver protein as a urethral irrigation. The duration of use was reported to have been 6 weeks.)

Re-examination and continuation of treatment. Few of the patients adhered, without lapse, to the schedule of return for re-examination and continuation of treatment that was requested of them. This schedule required, in the absence of recurrence, a total of 8 reports to the clinic; weekly during the month of treatment; at 3 week intervals during the next 2¼ months; and, again, 3 months later. *Treatment was not interrupted during the menstrual period.*

Following each re-examination during the period of treatment, an additional insufflation was given and 6 additional capsules, for use as before, with instructions to return again for examination at the end of the week, etc.

As is reported in Table I, the infections with an initial classification of +++ or ++++ required longer treatment on the average than those with an initial classification of + or ++, and had a greater tendency to recur. The number of weeks of treatment given, in the absence of recurrence, was between 3 and 4 and, in the presence of 1 or at most 2 recurrences, between 5 and 7. The percentage of patients successfully treated was 98.

The outcome, in the unsuccessfully treated patients, was one suggesting failure, not on the part of the therapeutic agent but of the precaution against reinfection (Fig. 5).

Results approximately equivalent to those obtained by the combined use of insufflation and capsule insertion were observed following

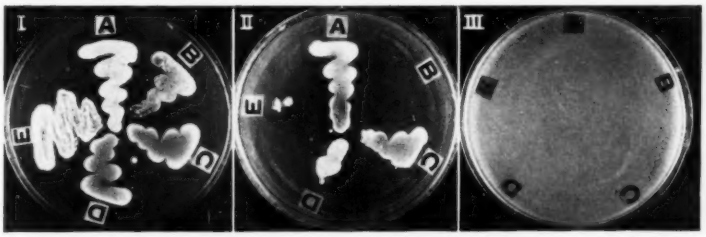

Fig. 6. Comparative bacteriostatic power of the argyrol kaolin, lactose powder against gram-positive Staphylococcus aureus, A; and Streptococcus pyogenes, B; and gram-negative Escherichia communior, C; Pseudomonas aeruginosa, D; and Eberthella typhosa, E. Tests made by a modification of the agar streak plate dilution method described by Waksman and Reilly.

Agar plates containing: I, no argyrol, kaolin, lactose powder; II, the powder in a dilution of 1:5000; and, III, in a dilution of 1:500. Note the complete restraint of growth at 1:500 and the marked restraint even at 1:5000.

the use of capsules alone. However, the return of the patient for insufflation provides for an automaticity of re-examination and control not possible through the use of capsules alone.

A study was made by one of us (M. J. N.) of the rate of disintegration and dispersion of the capsule following its placement high in the vaginal vault. Hourly observations were made and the process was found to be rapid, resulting in an apparently uniform distribution of the contents throughout the vagina within 3 to 4 hours.

MODE OF ACTION

The action of the powder would appear to be of the type exerted by the sulfonamides and by penicillin against the infections for which they are most effective—a mild, checking action, gradually depriving the pathogen of its foothold. Mild silver protein has been demonstrated to exert an additional germicidal effect, but that effect is secondary in importance to the checking effect imposed. A direct killing of Trichomonas vaginalis by 0.5 per cent mild silver protein *in vitro* has been observed by Shelanski which was reported to be complete in 8½ minutes. Morgan and Campbell observed a similar effect by 1 per cent mild silver protein versus Trichomonas foetus. Bucca found mild silver protein to be lethal for the gonococcus in a dilution of 1:50,000.

The photographs in Figure 6 indicate, graphically, the extent to which mild silver protein-kaolin-lactose powder checks the growth of representative gram-positive and gram-negative bacteria. There would seem to be little question of its capacity to control either Trichomonas vaginalis or the disturbed bacterial flora associated with it in the production of Trichomonas vaginalis vaginitis.

DISCUSSION

In our clinic, we have tried and had experience with all of the classical approaches to the treatment of Trichomonas vaginalis vaginitis.

TABLE 1.—DURATION OF TREATMENT IN RELATION TO INITIAL CLASSIFICATION AND FREEDOM FROM SOURCES OF RECURRENCE

Group	Initial classification	Number of recurrences	Number of cases	Average total no. of weeks of treatment	Per cent of group responding successfully to treatment
Negro	TV+,++	0	30	2.7	
		1	3	6.7	
	TV+++, ++++	0	35	3.7	
		1	8	5.3	
		multiple	2	—*	
	Combined		84		97.6
White	Series A†	0	19	3.5	
		1–2	4	6.0	
	Series B†	0–2	45	3–4	
		multiple	1	—*	
	Combined		69		98.6

*Not responding effectively. Indication for further search for source of recurrence rather than extension of treatment.

†Series A: clinic patients; Series B: office patients, studied over the same period.

Cleansing the external genitalia with tincture of green soap and warm water, with drying of the vaginal tract followed by treatment with a stream of warm air, has proved to be time-consuming and cumbersome, with fractional results even though trichomonadicidal agents were applied following the procedure and prescribed nightly for the patient. The substances used for this purpose were: picric acid (1 per cent), methylene blue (1 per cent), gentian violet (2 to 5 per cent), and saturated solutions of sodium perborate.

Various types of insufflation powders were explored, containing pentavalent arsenicals or silver picrate. Supplementary to the use of these preparations in the clinic, the patient nightly, at home, used the same drugs in tablet or suppository form. An acid douche, usually vinegar, was also prescribed twice a day, mornings and afternoons along with the clinic and home medication. Quinine sulfate, oxyquinoline sulfate, and the lactic acid, oxyquinoline jellies also were given thorough trial.

Fairly good results followed from the use of all these procedures, with, however, failures which led to a review of basic principles and the development of the method of approach described.

Work of others. A thorough review of the background of the problem appears in the report of the American Medical Association Council on Pharmacy and Chemistry on status of treatment of Trichomonas vaginalis vaginitis (10). Authoritative conclusions on the pathogenicity of Trichomonas vaginalis have been brought forward by Trussell and Plass, Hesseltine, and Feo, Rakoff, and Stabler (5). Comprehensive information on incidence is given by Peterson.

SUMMARY

A combined use of mild silver protein, kaolin, and beta-lactose in powder and vaginal capsule, together with search for and elimination of foci and sources of reinfection, gave a successful result against Trichomonas vaginalis vaginitis in 97.6 per cent of a group of 84 negro patients and 98.6 per cent of a group of 69 white patients, studied under both clinic and office conditions and with infections varying in initial severity and extent over the usually encountered range.

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EXTENSIVE HEMANGIOMA

Report of Cases

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REPORTS appear in the literature of extensive hemangiomas for which multiple or radical operations have been performed for their cure. Since the lesion, although rarely malignant, progressively enlarges, the necessity for its removal is apparent. Many methods of therapy have been instituted, but only in those instances which result in the total eradication of the lesion can one hope for permanent success. At the onset these lesions may produce only cosmetic deformities but eventually functional impairment and pain will result. Hemorrhage, malignant degeneration, and progression to true cirsoid aneurysms are further indications for radical extirpation.

PATHOLOGY

Hemangiomas are tumors of independently growing blood channels which probably have their origin as embryonic rudiments of mesodermal tissue. The concept that they result from dilatation of blood vessels or organization of hemorrhage has long been discarded (5, 7).

From the Vascular Surgery Center, Ashford General Hospital, White Sulphur Springs, West Virginia, and the Department of Surgery, Emory University.

Classification is usually of two types: cavernous hemangioma, and capillary hemangioma. The point of division between the two types is frequently difficult unless the specimen is carefully examined before fixation. Watson and McCarthy have classified them into eight groups; (1) capillary hemangioma, (2) cavernous hemangioma, (3) angioblastic or hypertrophic hemangioma, (4) racemose hemangioma, (5) diffuse systemic hemangioma, (6) metastasizing hemangioma, (7) nevus venosus or port wine stain, and (8) hereditary hemorrhagic telangiectasis.

The microscopic picture is one of endothelial spaces of varying size surrounded by interstitial connective tissue (Fig. 1). The amount of lipoid and fibrous tissue varies markedly; the proportion of these elements will determine the compressibility and consistency of the mass (Fig. 2). Many of them have the appearance of lipoma. It may be well encapsulated occupying a position between muscle

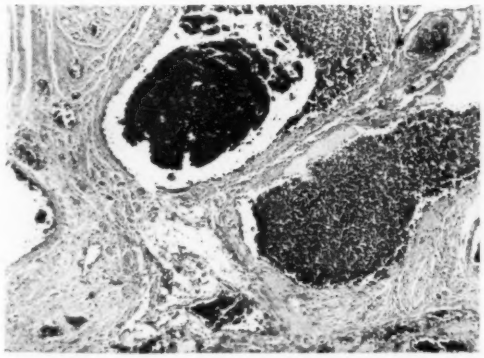


Fig. 1. Photomicrograph of a typical cavernous hemangioma.

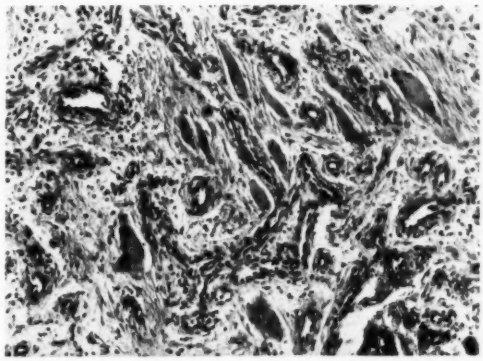
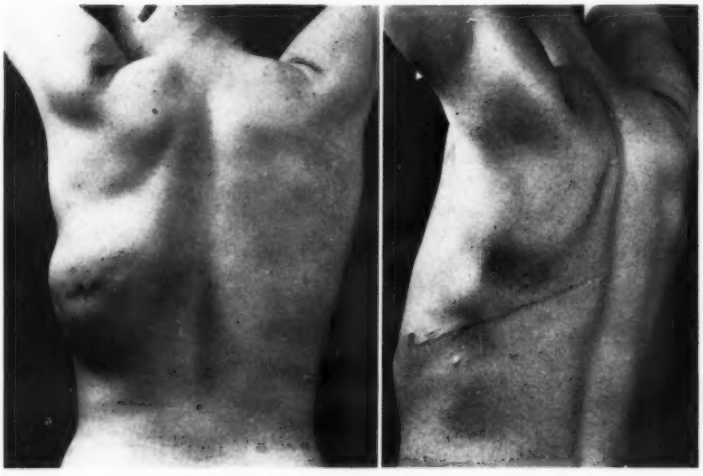


Fig. 2. Photomicrograph of a hemangioma with large amount of connective tissue and small vascular channels.

a b

Fig. 3.



a c

Fig. 4.

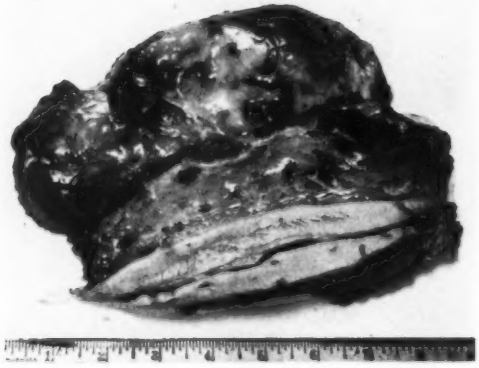
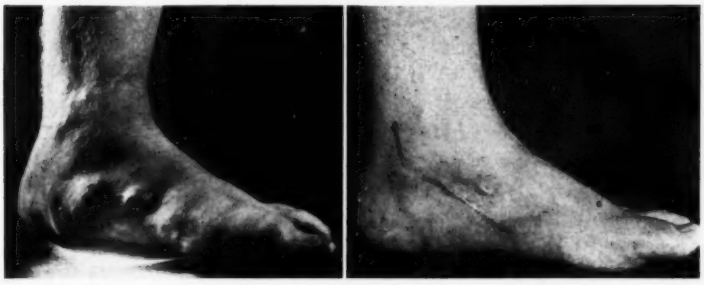


Fig. 4b.

Fig. 3. a, Hemangioma involving all muscles of the shoulder girdle. b, Postoperative result after excision of the major portion of the mass.

Fig. 4. a, Hemangioma involving the latissimus dorsi muscle. b, Specimen removed showing extensive deposition of fat about the vascular channels. c, Postoperative result after complete excision.



a b

Fig. 5. a, Hemangioma of foot with large veins leading from the tumor. b, Results after excision.

planes, or it may infiltrate adjacent muscles, nerves, or glandular structures.

The feasibility of complete excision of hemangiomas can be determined only by surgical exploration since the external appearance of the tumor is deceptive.

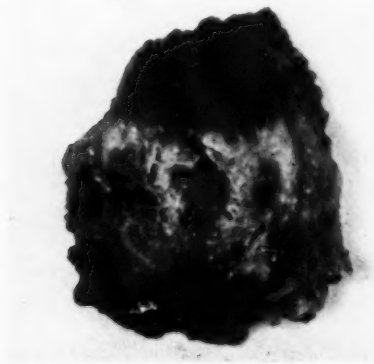
Hemangiomas usually occur on the face, back, or shoulder region, but may occur in any portion of the body. The lower extremities are more rarely affected than the trunk or upper extremities. Thromboses with the formation of phleboliths are common.

DIAGNOSIS

The diagnosis of extensive hemangiomas is not difficult. A mass of variable consistency is present which is compressible and which will re-expand after the involved part is compressed or when the large veins leading from it are occluded. On expansion the patient may complain of a feeling of fullness, heaviness, or pain. The rapidity of filling following compression is dependent upon the size of the arterial components.

Lesions about the face are best examined with the patient in the horizontal position with the head depressed. The mass will then be seen to enlarge, particularly if the jugular veins are occluded by pressure (Fig. 9). The presence of a "port wine" stain overlying the mass or infiltration of the overlying skin further substantiates the diagnosis. A bruit will not be heard unless large arteriovenous communications are present.

a c



b

Fig. 6. a, Hemangioma of vastus lateralis muscle. b, Cross section of specimen showing large vascular spaces. c, Postoperative result with minimal impairment of function.

Fig. 7. a, left, Hemangioma of forearm with rapid growth. b, Result after excision.

Following trauma or thrombosis of a major venous channel leading from the tumor, rapid enlargement may occur. The tumor then may become painful and simulate an acute inflammatory process.

Due to the variation in consistency and compressibility of the mass other conditions such as large dilated varices, lymphangiomas, and lipomas are to be differentiated from it. The deposition of fat about the vascular channels may be so great as to give the tumor the appearance of a lipoma even at the time of operation; in occasional instances the expansile quality may be absent. The true nature of the tumor is then appreciated only if it is incised exposing the vascular spaces. A lymphangioma may be compressible but is reduced in size less readily and expands less rapidly when released. Large masses of varices confined to a single area are differentiated by the greater ease with which they are emptied on compression and by the tests for varicose veins.

TREATMENT

Complete removal of the tumor is the ideal treatment. This is not always possible, for in lesions about the head loss of facial expression may result from associated injury to the facial nerve; extensive removal of muscles about an extremity may destroy the function of the part, and at times the major nerves are so intimately involved in the process that removal of the tumor without injuring them is not possible. It is believed that in so far as it is compatible with essential functions of the individual, every attempt should be made completely to excise the lesion, for these tumors increase steadily in size and frequently undergo changes of distressing or even fatal nature.

Excision. All cases in this series were treated by excision. The overlying skin was excised if it was involved, and if a satisfactory closure could not be obtained skin grafting was done.

Irradiation was employed only in instances in which surgical excision was inadvisable or incomplete after exploration of the lesion. The use of sclerosing solutions would seem futile in large cavernous tumors and such treatment was not employed.

Review of cases (Table I). In the cases reported in this series all patients were treated by surgical excision. Many other hemangiomas were seen but those of small size and

Fig. 8. a, left, Hemangioma of hand with involvement of intrinsic musculature, median and ulnar nerves. b, Postoperative result after excision of a portion of the mass.

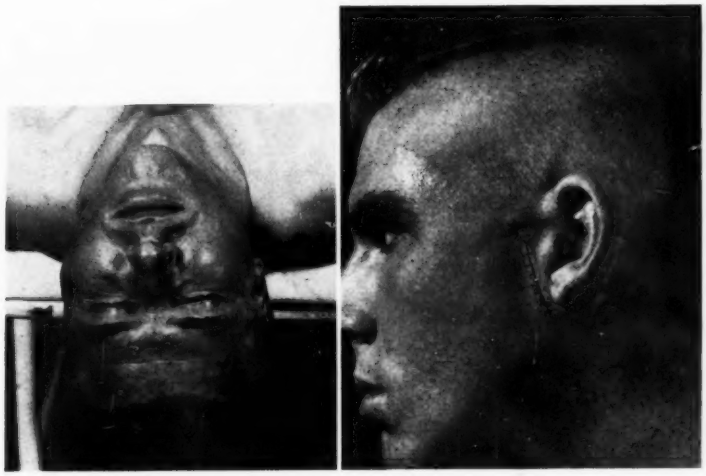


Fig. 9. a, left, Hemangioma of parotid region and temporal muscle with expansion as head is depressed. b, Photograph following partial excision of the tumor.

involving only the skin are not included. Other instances of "port wine" blemishes involving large areas were not excised. Tumors of the parotid region, except for 1 instance in which it was believed that the mass was superficial, were uniformly referred for irradiation therapy.

History of trauma was present in 14 cases. It is believed that trauma is frequently the factor initiating increased growth in an underlying congenital lesion.

Pulsation was present in 3 instances and in 2 of these a bruit was audible, and was interpreted as evidence of large arteriovenous communications.

In 1 instance the median and ulnar nerves were infiltrated making excision impossible without removing the nerves.

Fig. 10. a, left, Hemangioma of frontalis muscle with communicating diploic veins. b, Postoperative result showing method of reflecting flap to permit excision.

TABLE I.—REVIEW OF CASES

Case No.	Location	Birth mark		Trauma		Rapid enlargement		Skin involvement		Complete excision		Results	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Cured	Improved
1	Buttock and thigh		1	1		1		1			1		1
2	Parotid region		1		1	1			1		1		1
3	Chest wall		1	1		1			1	1		1	
4	Cheek	1		1		1		1			1		1
5	Hand and wrist		1	1		1			1		1		1
6	Forearm		1	1		1			1	1		1	
7	Calf of leg		1	1		1			1	1		1	
8	Fourth finger and hand	1		1			1	1		1		1	
9	Axilla and chest wall	1		1			1	1		1		1	
10	Scalp		1	1		1		1		1		1	
11	Arm		1		1	1			1		1		1
12	Foot	1		1		1		1		1		1	
13	Cheek		1		1		1		1	1		1	
14	Scalp and ear		1	1		1		1		1		1	
15	Chest wall		1	1		1		1			1		1
16	Leg	1		1		1		1		1		1	
17	Thigh		1	1		1			1	1		1	
18	Cheek		1		1	1			1	1?			1
19	Forehead		1		1	1			1	1		1	
	Total	5	14	11	5	16	3	9	10	13–1?	6	12	7

In 12 instances the tumor was completely excised. In 7 the mass was removed but a small amount was left; 1 case involved the masseter muscle alone and although this muscle was removed the complete extirpation of the origin of the muscle was not confirmed. All muscles of the shoulder girdle were infiltrated in 1 instance and the tumor could not be removed without sacrificing the arm. In 2 instances the masseter and temporal muscles were involved and left after excision of the major portion of the mass. The remainder of the failures were associated with extensive "port wine" blemishes in which the expansile portion of the tumor was removed but in which it was not felt justifiable to do widespread skin excision. Postoperative irradiation therapy was employed in 3 patients.

SUMMARY AND CONCLUSIONS

1. Nineteen cases of extensive hemangiomas treated by surgical excision are reported.

2. The preoperative evaluation of the probability of complete removal is difficult because of the fact that the tumors are deceptive as to extent and involvement of adjacent structures.

3. Cures were effected in 63 per cent of cases and improvement obtained in the remaining 37 per cent.

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THE CHOICE OF OPERATION FOR THE TREATMENT OF ARTERIOVENOUS FISTULAS

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QUADRUPLE ligation with excision of the fistula has been the classical operation in the treatment of arteriovenous aneurysm for many years. Holman, Herrmann and Reid, and Elkin have advocated this procedure as being the most useful and effective technique. Recently, however, reports have appeared which indicate that although patients treated in this manner may not develop gangrene after operation, nevertheless a good many of them will show evidence of chronic vascular insufficiency distal to the ligated vessels. Symptoms such as intermittent claudication, ischemic pain, numbness, tingling, atrophy of muscles, or coldness of the skin, may develop to plague the patient even though a successful quadruple ligation has been accomplished. Mayberry, Bigger, and Freeman all have stressed that these untoward postoperative conditions may be avoided by closure of the fistula and repair of the artery. In a recent report, Heringman, Rives, and Davis studied 53 cases of arteriovenous fistula for evidence of postoperative vascular insufficiency. It was found that there was no instance of vascular inadequacy following transvenous arteriorrhaphy as compared to an incidence of 27.5 per cent following quadruple or sextuple ligation, and an incidence of 71 per cent following obliterative endoaneurysmorrhaphy. It was stressed that "restoration of normal arterial circulation is the primary objective of the surgeon whenever possible."

Unfortunately, there exist at the time of operation many complicating conditions which may prevent the repair of the artery. Therefore, one must resort all too frequently to quadruple ligation or at times to obliterative endoaneurysmorrhaphy in order to eliminate the fistula. It is the purpose of this paper to discuss those factors which are the basis for the choice of operation in a patient with arteriovenous fistula. Although these factors are known to the vascular surgeon, relatively little has been said about them in recent discussions, and it is considered worthwhile to re-emphasize their importance. Certain appropriate cases taken from the group of 53 analyzed in the original paper (7) are used as examples to illustrate how these factors influence the choice of operation.

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OPERATIVE PROCEDURES

In general, there are three main types of operative technique available to the surgeon when dealing with an arteriovenous aneurysm. The first and most frequently used is a ligation procedure, either quadruple or sextuple ligation with excision. The second is a restorative procedure utilizing some method of arteriorrhaphy or a technique requiring the use of vitallium tubes with a venous graft (3). The third is an obliterative procedure, the intrasaccular endoaneurysmorrhaphy advocated by Matas (10).

The advantages and disadvantages of these procedures merit a brief discussion.

LIGATION PROCEDURES

Quadruple ligation with excision. The advantages of this operation are derived from the fact that when properly performed, it is a relatively safe procedure and effectively eliminates the fistula without causing gangrene. It is frequently the operation to which one must resort if a restorative procedure cannot be done. However, there are certain definite disadvantages inherent in this operation:

1. It requires ligation of the main arterial pathway, which should not be done unless it is absolutely necessary.

2. Dissection around the sac necessitates ligation of some collaterals which may be essential for maintenance of blood flow to distal parts.

3. The dissection of the sac is often time-consuming, requiring the ligation of innumerable bleeding points caused by increased pressure in the veins around the fistula.

4. It is not physiological.

5. It is followed in many cases by evidence of postoperative vascular insufficiency.

Sextuple ligation. This is a procedure required for an arteriovenous fistula which occurs between an artery and its two venae comitantes. It is fundamentally a ligation and excision operation with disadvantages which theoretically do not differ from those mentioned under quadruple ligation and excision. However, this technique is ordinarily the only one of advantage in the presence of dual fistulas.

RESTORATIVE PROCEDURES

Transvenous arteriorrhaphy (Matas-Bickham, 1). This procedure is performed without difficulty if the fistula occurs in a region where the blood supply can be controlled either by a proximal constrictor or by temporary ligatures on the artery and vein proximal and distal to the fistula.

The advantages of this operation are well known:

1. It preserves the main arterial pathway, which is especially important in certain regions such as those supplied by the common carotid, internal carotid, and popliteal arteries.

2. It provides a rapid approach to the fistula, which can then be closed under direct vision.

3. There is minimal interference with the collaterals because little dissection is required around the fistula or the sac.

4. Patients who can be treated successfully by this method show little evidence of postoperative vascular insufficiency.

Disadvantages inherent in this procedure stem chiefly from local contraindicating factors, which become apparent only at time of operation.

1. It requires an arterial wall which has not undergone advanced pathologic change and has not become involved in dense scar tissue. (The presence of such findings creates insurmountable technical difficulties.)

2. Sufficient normal arterial wall must be present in order to permit closure of the fistula without a serious reduction in the lumen of the artery.

3. It requires control of circulation, which at times may be difficult or impossible to obtain.

4. Occasionally the repair of the artery will result in a marked reduction or even complete obliteration of the lumen. This is a technical error, and every effort should be made to avoid it.

5. Should postoperative infection supervene, the suture line may give way, causing serious secondary hemorrhage.

6. Occasionally recurrence may follow restoration of the arterial pathway. This complication has been reported by Reid, Pemberton and Black, Bigger, and Freeman.

7. Thrombosis of the artery may occur at the site of repair.

8. Unless the artery is exposed completely and carefully examined, a weak point in the arterial wall may be overlooked, which may result in the subsequent development of an aneurysm.

Transverse suture. This technique has been advocated recently by Freeman. Since both artery and vein must be completely exposed to permit their detachment at the site of the fistula, there is little likelihood that a weakened area in the artery will be overlooked.

This complete exposure of artery and vein is an advantage over transvenous suture because with a direct approach to the fistula through the vein, complete exposure of the vessels is not necessary and a pathologic area in the arterial wall can be easily overlooked. Another advantage of this procedure has been demonstrated by Freeman, who used this method of repair successfully even though the wound may involve as much as three-fifths of the arterial wall. Such a wide defect obviously cannot be eliminated by the transvenous technique employing longitudinal suture without encroachment on the lumen of the artery.

The disadvantages of this operation are essentially the same as those of transvenous arteriorrhaphy. Furthermore, a long slit-like opening between artery and vein cannot be closed transversely.

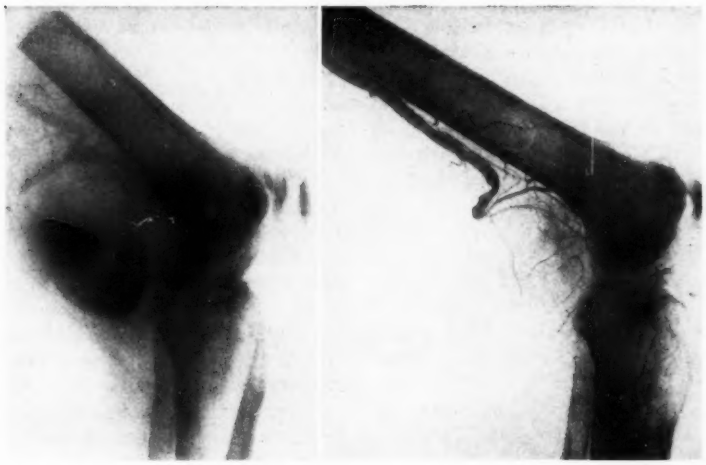


Fig. 1. a, left, Arteriogram taken of a patient of Dr. Urban Maes shows a large popliteal arterial aneurysm with the artery entering the upper pole. b, Arteriogram of same patient following an obliterative endoaneurysmorrhaphy. Note two large branches which have been preserved despite their origin close to the sac. If ligation of the artery had been done, these collaterals undoubtedly would have been lost.

Vitallium tube-venous graft method (Blakemore and Lord). The development of this technique offers a new approach to the problem of restoring the artery to normal function. It seems advantageous for the following reasons:

1. It permits complete excision of the fistula, sac, and that portion of the artery which has undergone pathologic change.
2. Despite excision of the involved segment, the main artery is restored to function by means of a venous graft.
3. It is relatively simple and does not require suturing of blood vessels.
4. It is actually a combined quadruple ligation and restorative procedure, thus presenting the advantages of both.

The disadvantages of the operation may arise from the fact that dissection of the sac and fistula may seriously interfere with collateral circulation. Because of this, vascular insufficiency may result if early thrombosis should occur in the venous graft.

OBLITERATIVE PROCEDURES

Intrasaccular obliterative endoaneurysmorrhaphy, designed primarily for the treatment of true or false aneurysms, has also been used successfully in the treatment of arteriovenous aneurysms. This operation requires adequate proximal control of circulation by a constrictor.

The advantages of this procedure are:

1. It cures the fistula.
2. It preserves the collaterals because no dissection is required around the sac. Figure 1 shows an example of how collaterals are preserved by this method.
3. It is extremely useful in the presence of a large sac with numerous communications.

The disadvantages of this procedure are:

1. It obliterates the main arterial pathway.
2. It can be done only in an area where proximal control of circulation by a constrictor is possible.
3. It may be followed by a high incidence of vascular insufficiency.
4. The lesion may recur if one of the openings in the sac is overlooked or if one of the suture lines breaks down.

CHOICE OF OPERATION

The decision as to what technique should be used is frequently difficult. Since no two cases are alike, a number of complicating conditions present themselves at operation and require individual consideration.

The great variability of these factors prevents any attempt at rigid classification. However, a satisfactory division can be made by grouping them under two main headings, depending on whether they are local or general in nature. The classification as presented in Table 1 indicates the more important factors.

TABLE 1.—FACTORS INFLUENCING THE CHOICE OF OPERATION

Local factors	General factors
1. Scarring around the vessels secondary to the original trauma.	1. Cardiac status of the patient.
2. Local pathologic changes in the walls of the involved vessels.	2. Presence of generalized arteriosclerosis.
3. Anatomic location of the fistula.	3. Occupation of the patient.
4. Factors relative to the aneurysmal sac.	
a. Presence and location of the sac in relation to the fistula.	
b. Size of the sac.	
c. Condition of the sac wall.	
5. Collateral circulation.	

Local Factors

Scarring around the vessels secondary to the original trauma. Here the nature of the injury and the presence of coincident infection are important. If the walls of the vessels or of the sac are involved in dense scar tissue, dissection is often hazardous and may produce severe hemorrhage. Matas (11) points out that repair of the artery is practicable only in recent injuries in which adhesions are not so dense as to prevent mobilization of the vessels. One of the cases in the series previously reported exemplifies the difficulties that may occur because of dense scarring found at operation.

CASE 1. A. B. was admitted to Touro Infirmary in 1938, with an arteriovenous fistula of the left common femoral vessels resulting from a gunshot wound of the left groin incurred 11 years earlier. At operation, a considerable amount of scarring was found involving the walls of the vessels as well as the surrounding tissue. Dissection of the vessels in the region was attempted but accidental opening was made into a large venous channel. The ensuing hemorrhage was so severe that the operation was discontinued, and a pack placed in the wound for hemostasis. About 10 days later ligation of the external iliac vessels was performed. After removal of the pack from the original operative wound, severe infection developed, causing profuse secondary hemorrhage, which was controlled with difficulty. The patient ran a markedly septic course for approximately one month and finally recovered. Fortunately, evidence of the fistula disappeared and the patient was discharged from the infirmary with no further complications.

The choice of operation was determined by the local factors. The technique was an improvisation at best. Ligation of the external iliac vessels eventually produced a cure, but secondary infection, thrombosis, and thrombophlebitis probably were contributing factors in the disappearance of the fistula. This also serves to emphasize the importance of obtaining control of the proximal and distal circulation before dissection in the area of the fistula is begun. If temporary control of circulation can be achieved before the fistula is attacked directly, unfortunate complications may be frequently avoided.

Presence of local changes in the wall of the involved vessels. This factor must be carefully determined before a decision can be made as to the proper procedure. When pathologic changes occur in the arterial wall, such as marked thinning and dilatation, calcification, or fibrosis, transvenous arteriorrhaphy may be dangerous. In such cases, quadruple ligation and excision of the involved vessel segments with the fistula is the procedure of choice. This is exemplified in the following case.

CASE 2 (Fig. 2). A. M. was admitted to Touro Infirmary with an arteriovenous fistula of the popliteal vessels as a result of a gunshot wound incurred 3 months earlier. When the wound was explored considerable scarring was found, and the wall of the artery opposite the fistula was thin and bulging. The fistula and the involved vessels were isolated by careful dissection and the lesion excised by means of a quadruple ligation. The patient suffered no untoward effects postoperatively.

Obviously arterial repair in this case would be hazardous because of the weakened arterial wall. Even if arteriorrhaphy could be accomplished, the thinned area would remain as a possible site for early rupture with dangerous secondary hemorrhage or late aneurysmal dilatation.

The anatomic location of the fistula. The relationship between proximity of the fistula to the heart and subsequent development of car-

Fig. 2. Arterial wall opposite the site of fistula was thin and bulging. Quadruple ligation and excision of the fistula with the weakened portion of the artery was performed.

diac changes is too well known to merit more than a passing reference. Management of the local lesion, however, will vary according to the vessels involved. For example, a lesion of either one of the main arteries at the wrist can be treated by ligation and excision, because there is always an adequate secondary arterial circulation. This is also true of other regions where collateral circulation is known to be adequate.

On the other hand lesions of large main vessels present a much more serious problem. The choice of operation for a fistula involving the common or the internal carotid artery requires careful judgment. Collateral circulation usually does not develop satisfactorily in such cases, and with a quadruple ligation or obliterative procedure there is always the risk of hemiparesis, especially in older individuals. This unfortunate complication can often be avoided by a procedure designed to restore the arterial pathway. Arteriorrhaphy whenever possible is always preferable in the presence of a fistula involving the common or internal carotid artery. The following case demonstrates the suggested method of handling such patients.

Case 4. L. M. entered Charity Hospital with an arteriovenous fistula of the right common carotid artery and internal jugular vein, caused by a gunshot wound incurred 7 weeks prior to admission. Three weeks later a modified transvenous repair of the fistula was performed, with reconstruction of the carotid artery and the ligation of the internal jugular vein above and below the fistula. Heparin was administered after operation and a hematoma developed rather promptly. This was evacuated and the

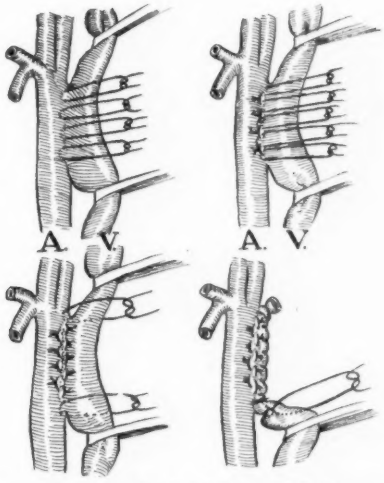


Fig. 3. Diagrammatic sketch of a modified transvenous arteriorrhaphy. In order to avoid tearing the internal jugular vein, complete liberation from surrounding scar tissue was not attempted. Instead large U mattress sutures were placed across the fistulous opening and tied. The vein was then interrupted above and below the fistula and the wall sutured to reinforce the closure of the fistula.

remainder of the postoperative course was uneventful. The patient was discharged fully recovered, with no evidence of cerebral vascular deficiency. Figure 3 shows the lesion and the method of repair which was used.

Fistulas of other large vessels also merit a determined attempt at restoration of the arte-

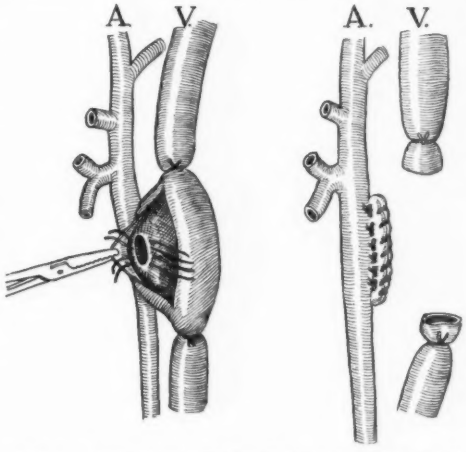
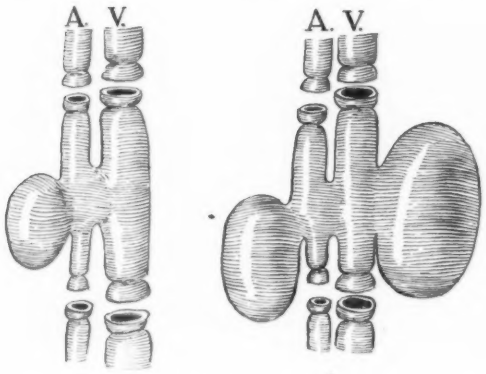


Fig. 4. Transvenous arteriorrhaphy with section of vein proximal and distal to fistula.



a b

Fig. 5. a, Quadruple ligation and excision of the sac with involved artery and vein. b, Quadruple ligation and excision of both sacs with the involved artery and vein.

rial lumen. This applies especially to lesions of the brachial, common femoral, and popliteal vessels.

Factors relative to the sac. The simplest type of communication is one in which there is a direct opening between artery and vein, with no intervening sac. This type of lesion is best treated by transvenous repair. Proximal and distal control of circulation can be obtained easily. The transvenous closure of the fistula is accomplished through the vein, restoring the artery to normal function and leaving collaterals undisturbed (Fig. 4).

There is often a false aneurysmal sac present in connection with the fistula. In such cases so much of the arterial wall has disappeared that repair is impossible. Quadruple ligation with excision or an intrasaccular obliteration may be used, depending on the other factors mentioned previously.

CASE 5 (Fig. 5a). J. S. was admitted to Charity Hospital with an arteriovenous fistula of the right superficial femoral vessels caused by a gunshot wound in the thigh inflicted 18 years before. At operation a large rent, incorporating more than half the diameter of the artery, was found between the artery and vein. In the arterial wall, opposite the fistula, there was a small aneurysmal sac. Because very little normal arterial wall was left, a quadruple ligation with excision was performed. There were no postoperative complications.

CASE 6 (Fig. 5b). A. C. was admitted with a long standing arteriovenous fistula of the left common femoral vessels. At operation two large false sacs were found opposite the fistula, one communicating with the artery, the other with the vein. In this case, too, a quadruple ligation with excision was performed because so little of the normal arterial wall remained.

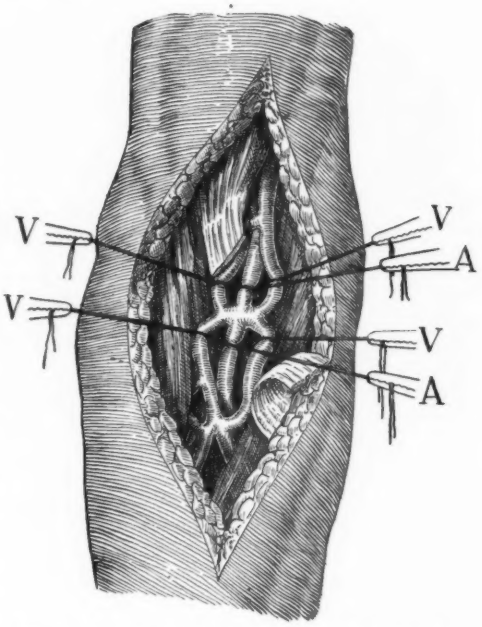


Fig. 6. Sextuple ligation with excision of involved portion of the artery and veins.

In the presence of dual fistulas between the artery and the two venae comitantes, an operation designed to restore the arterial lumen is usually contraindicated because too much of the arterial wall has been destroyed and because the caliber of the artery is often too small to merit an attempt at repair.

CASE 7. M. I., admitted to Touro Infirmary, was found to have an arteriovenous fistula of the ulnar vessels caused by a stab wound of the left wrist. At operation sacculations between each of the vessels were found. A sextuple ligation with excision was easily accomplished, with no subsequent complications (Fig. 6).

A large aneurysmal sac with a number of communicating arterial and venous channels makes a restorative operation practically impossible. As a rule, the wall of the artery becomes part of the sac and undergoes marked changes, adding to the operative difficulties. If such a sac is located in a region which would

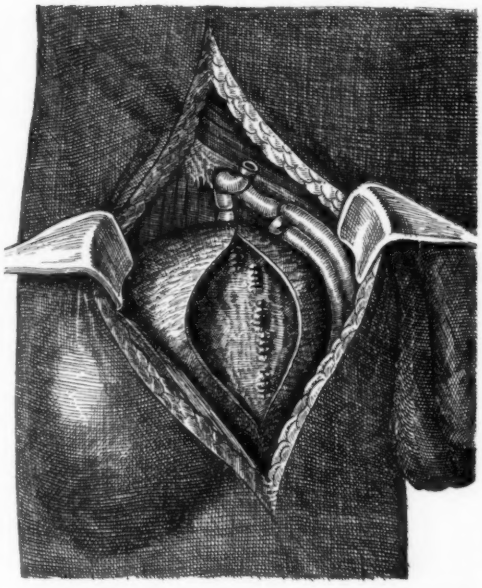


Fig. 7. Intrasaccular obliterative endoaneurysmorrhaphy. A proximal constrictor could not be used because the lesion was too close to Poupart's ligament, making the operation exceedingly difficult. Fortunately, a Matas-Allen aluminum band which had been placed around the profunda femoris artery controlled the bleeding sufficiently to permit successful conclusion of the operation.

permit the use of a proximal constrictor, an obliterative endoaneurysmorrhaphy is the operation of choice, because dissection around the sac in the effort to extirpate it, even if technically possible, would invariably result in marked interference with collateral circulation. Obliterative endoaneurysmorrhaphy attains its maximum usefulness in the treatment of a case such as the one recently described by Rives.

CASE 8. A. C. was admitted to Charity Hospital with an arteriovenous aneurysm of 6 months' duration, caused by a gunshot wound of the left thigh. A huge false aneurysmal sac developed, extending from Poupart's ligament to the lower third of the thigh. It contained fully 2 liters of blood at the time of operation. The superficial femoral artery and vein were ligated before it could be ascertained that the sac and fistula involved the profunda femoris. This was an error resulting from the fact that the external iliac artery bifurcated above Poupart's ligament and the superficial femoral and profunda femoris passed separately into the thigh. An intrasaccular obliterative endoaneurysmorrhaphy was performed in the

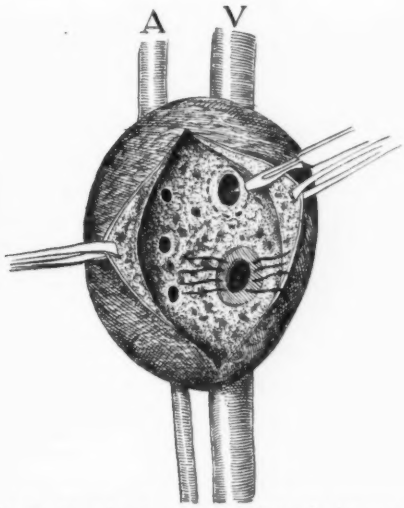


Fig. 8. In order to preserve collaterals, intrasaccular obliterative endoaneurysmorrhaphy can be accomplished despite calcification of wall of the sac by utilizing this method. A disc of calcified wall is excised around each opening in the sac and the fibrous tissue underneath can then be used to close the opening accurately.

effort to preserve as much of the collateral circulation as possible. If an attempt had been made to dissect out the sac and ligate its various connecting vessels, the patient, in all probability, would have been lost because of hemorrhage. Certainly most of the collateral circulation to the leg would have been destroyed. By working within the sac, it was possible to suture the seven openings into the sac and preserve a maximum number of collaterals (Fig. 7). The patient made an uneventful recovery, although edema of the limb persisted for several months.

If the sac has undergone degenerative changes with deposition of calcium salts, operations requiring suture through the calcified areas are contraindicated. Bigger considers calcification of the wall of the artery as the most important contraindication to arterial suture. In such instances, it is preferable to perform a quadruple ligation with excision.

CASE 9. W. D. was admitted to Touro Infirmary with an arteriovenous fistula of the right femoral vessels of 1 year's duration. At operation the artery and vein were found to form a fusiform dilation in the middle of which was an opening measuring 0.5 centimeter in diameter. There was a deposit of fine calcified material in the walls of this saccular enlargement. Therefore, a quadruple ligation with excision of the fistula and sac was performed, without subsequent complication.

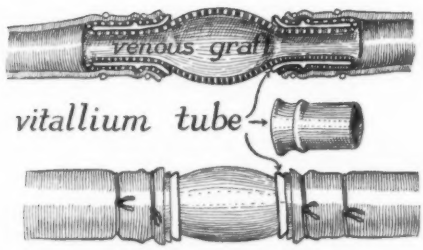


Fig. 9. Blakemore-Lord technique utilizing a venous graft and two vitallium tubes.

If the collateral circulation in this patient had been found inadequate, an obliterative endoaneurysmorrhaphy could have been done in an effort to preserve as many accessory vessels as possible. To avoid suturing through an area of calcification, a disc of calcified sac wall is excised around each opening. This will ordinarily leave enough fibrous tissue to permit closure of the openings in the usual manner. Figure 8 illustrates this modified technique.

Collateral circulation. The type of operation required in a given case must to a great extent depend on the adequacy of the collateral circulation. Collateral vascular channels will usually develop to a remarkable degree around an arteriovenous fistula if sufficient time is allowed to elapse. The time factor is all important. In those patients that present themselves to the surgeon quite early, it is essential to postpone operation long enough to permit the establishment of good circulation in accessory vessels. However, there are two important complications which require early operative intervention despite a doubtful collateral circulation. These are: (a) progressive edema and hemorrhage in the tissues around the fistula, producing pressure sufficient to cut off the collateral circulation and threaten the development of gangrene, and (b) early cardiac decompensation.

In the presence of a rapidly enlarging hematoma with compression of the collaterals, the usual operation is quadruple ligation with excision. This procedure will stop the bleeding, remove the fistula, evacuate the clot, and relieve the tension. The surgeon can only hope that the collaterals present at the time of operation will be sufficient to prevent ischemia or gangrene. Restorative procedures or obliterative procedures as a rule cannot be done in such instances.

However, it must be remembered that ligation of the main artery in the face of poor collateral circulation is not satisfactory. One case aptly demonstrates the complications that may occur when quadruple ligation and excision is performed before adequate collateral circulation has been established.

CASE 10. G. Y. was admitted to Charity Hospital suffering from a gunshot wound of the left thigh just below the inguinal ligament. An arteriovenous fistula of the common femoral vessels developed subsequently. Left lumbar sympathectomy was performed 3 weeks after admission, and operation for removal of the fistula was performed 2 weeks later. During operation the femoral artery was found to be involved by considerable scar tissue and was opened accidentally, resulting in a decision to perform a quadruple ligation. Postoperatively, despite sympathectomy, the patient's foot was cold and pulseless, and the leg became indurated, swollen, and painful. The patient had to stop smoking and required prolonged treatment with elastic bandages, bed rest, and elevation of the limb for months after operation. Apparently the 5 week waiting period between injury and operation was too short to permit formation of sufficient collateral circulation.

On the other hand, when early cardiac decompensation occurs before adequate collaterals develop, the surgeon is faced with an entirely different aspect of the problem. He must then direct his efforts toward eliminating the unprecedented load on the heart.

General Factors

Cardiac status. Impaired cardiac status may manifest itself either as early or late decompensation. Early failure as a result of arteriovenous fistula is relatively uncommon. This is probably due to the fact that larger arteriovenous communications, which immediately overload the heart, often require emergency operative intervention to prevent fatal hemorrhage. Despite the fact that there is not time for collaterals to develop, ligation and excision is the usual method used in the treatment of most of these cases. An obliterative endoaneurysmorrhaphy would not be feasible because a false aneurysmal sac requires some time to develop. Furthermore, owing to the marked inflammatory reaction in and around the vessels, incident to the trauma, sutures

may not hold at this stage, with the result that arterial repair would be technically difficult and hazardous. The technique using vitallium tubes with a venous graft gives the promise of being a useful operation under such circumstances (Fig. 9). Blakemore and Lord have reported considerable success with their elective cases. Unfortunately, recent papers by Rose, Hess, and Welch, and DeBakey and Simeone show that poor results were obtained when the nonsuture technique was used for war casualties with arterial injuries. More experience is necessary before the influence of this method can be accurately evaluated.

The development of cardiac symptoms late in the course of this condition is a frequent occurrence and has offered a fruitful field for many investigations. Those patients who show signs of decompensation with cardiac enlargement should be prepared for operation with utmost care. As a routine measure, repeated compression of the fistula preoperatively is advocated to permit adjustment of the heart to the circulatory changes which will occur after operation.

There will be occasional patients who have advanced cardiac disability as a result of a long standing fistula. Price recorded 5 such cases in 1937. Operation was considered impossible in 3 of these patients, and only an incomplete procedure could be done in the remaining 2. When myocardial damage is severe, a major operation is ill-advised. Under such circumstances ligation of the proximal artery and vein or the proximal vein alone may prove beneficial as a preliminary step. These are relatively simple procedures which can be performed under local anesthesia and by reducing the amount of blood pouring back to the heart, may produce temporary relief. If sufficient improvement then takes place, the patient will be able to withstand a second operation eliminating the fistula.

Fortunately, the cardiac changes in most instances are moderate and reversible. With careful preparation any one of the three main types of operative procedures can be used, depending on the other factors. In the final analysis, the cardiac status of a patient will greatly influence the choice of operation because the primary concern of the surgeon is to produce relief for the decompensated heart. Cure of the fistula then may become a matter of secondary importance.

Generalized arteriosclerosis. This causes degenerative changes not only in the vessels involved by the fistula but also in the collateral vessels. Repair of a calcified, arteriosclerotic artery is contraindicated, because of postoperative complications such as secondary hemorrhage, thrombosis, and further degeneration of the arterial wall, with subsequent formation of an aneurysm. Quadruple ligation is preferred in such cases despite the risk of poor collateral circulation.

Occupation of the individual. Patients who lead a sedentary life and who are rarely called upon to exercise the involved limb strenuously may do well with quadruple ligation. But as Blakemore and others have pointed out, strenuous exercise such as that which is experienced by a dancer or by a soldier will require an arterial pathway that is functioning normally.

CONCLUSIONS AND SUMMARY

1. Postoperative deficiencies in circulation frequently follow the use of quadruple ligation and excision in the treatment of arteriovenous fistula.

2. Recent reports indicate that restoration of the main arterial pathway is the primary objective and should be accomplished whenever possible.

3. There are a large number of variable factors which influence the choice of operation for arteriovenous fistula.

4. Some factors contraindicate any procedure which interrupts the arterial blood flow. Others contraindicate restoration of the arterial lumen.

5. The importance of certain factors, both local and general, have been discussed, and their relationship to the choice of operation has been considered, with appropriate cases used as examples.

6. There is no single operative procedure of choice for all cases of arteriovenous fistula.

7. The surgeon must be prepared to use any one of the standard procedures, or even an improvised technique in order to overcome individual problems which may be found at operation.

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THE ACTION OF UREA AND SOME OF ITS DERIVATIVES ON BACTERIA

IV. The Effect of a Mixture of Urethane and Sulfanilamide on the Bacterial Flora of Infected Wounds in Man

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THE failure of the topical application of the sulfonamides to eradicate bacteria completely from infected wounds has led to their use in combination with various other agents. Because of its ability to dissolve necrotic tissue, urea was one of the first agents proposed for combination with the sulfur-containing chemotherapeutic agents in the treatment of wound infections. Holder and MacKay (7, 8, 9, 10) demonstrated that a 10 per cent solution of sulfanilamide in saturated urea was very effective in infected wounds. It was thought to be nonirritating to tissue and not to impede healing. Urea itself was found to be bactericidal and, in addition, was shown by Tsuchiya, and his coworkers (21, 22, 23), by Lee, Epstein, and Foley and by Weinstein and McDonald (27) to inhibit the action of para-aminobenzoic acid. The literature on the use of urea sulfonamide combinations is extensive, and most of it has been summarized in the preceding papers of this series.

Neter and Schmelkes and Wyss have demonstrated the syngergistic action of azochloramide and sulfonamides, and have advocated the use of this combination in the treatment of infected wounds. A number of compounds including iodine, azochloramide, hydrogen peroxide, and other oxidizing agents were examined by Goldberger, who reported an increase in the chemotherapeutic activity of the sulfonamides when one of these substances was added.

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Urethane has been shown by Weinstein and McDonald (24, 27) to be bacteriostatic and bactericidal for gram negative bacteria. When added to sulfonamides, it was found to increase their bacteriostatic effects and solubility and to inhibit para-aminobenzoic acid. The antibacterial action of urethane was found to be greater against gram negative than gram positive organisms, large numbers of the former being killed by short exposures to a 10 per cent solution of the drug. Although Johnson (6, 11) claimed that urethane exerted an antisulfonamide effect on luminous bacteria, McIlwain, Martin and Fischer, and Weinstein and McDonald (25, 27), using different species of bacteria, could not confirm this observation.

Urethane (4) has the following structural formula: $O = C^{NH_2}_{OC_2H_5}$. It is closely related chemically to urea and carbromal and consists of colorless crystals which are soluble in water and alcohol. It is combined with quinine hydrochloride for the injection treatment of varicose veins and has been employed as a hypnotic in patients with asthma and during parturition. Its chief value is as an anesthetic agent in laboratory animals, but the hypnotic activity in man is too unpredictable for practical clinical usage. It is oxidized by the body to carbon dioxide and urea and is said to be nontoxic when administered orally in doses of 2 to 4 grams.

The purpose of the work reported here was to determine whether the highly specific antibacterial capacity of urethane against gram negative organisms, demonstrated *in vitro*, could be substantiated when this drug was used as a topical agent in surgical infections.

METHODS

Thirty-nine unselected cases of various types of surgical infections from the surgical services of three hospitals were used in this study. All of the cases were not followed through to their clinical end-results, emphasis being placed on the changes occurring in the bacterial flora of the wound when treated with the urethane sulfanilamide mixture. Some cases were abandoned because of inability to maintain sterility or to abolish the gram negative portion of the bacterial flora; these have been included as failures. The criterion for a response to treatment was the absence or presence of a change in the types and numbers of bacteria in the wound. It was impossible to exercise adequate surgical control in some of the cases.

A thorough history of each case was obtained, including the duration of the infection, prior surgery, and the duration and type of previous chemotherapy. In addition to a careful physical examination, a detailed description of the wound was recorded and the patient's age, dietary history, red blood count, hemoglobin, and serum protein level were used to classify the patient's physical status. Each infection was classified as acute or chronic. Follow-up notes were made, including the type, length of time, and complications of therapy rendered during this study, and an assessment of the adequacy of concurrent surgical treatment.

At the time of the initial dressing, a nurse was instructed in the proper procedure. Lack of optimal dressing conditions, unco-operative patients, and shifts in nursing personnel occasionally raised doubt as to the faithfulness of dressings, so that an opinion as to adequacy of urethane treatment was recorded for each case (Table I).

Cultures, taken at the time of the initial dressing and every 2 days thereafter, were planted on heart-infusion-blood-agar plates and in heart-infusion-blood broth, and incubated for 24 to 48 hours. Colony types were identified on the basis of specific diagnostic tests, and an exact bacteriologic diagnosis made in each case. A careful record was kept of the relative numbers of gram negative and gram positive bacteria in each culture, and the time of disappearance of each was noted.

Most of the patients were treated with a mixture of 10 per cent urethane and 1 per cent sulfanilamide. This was prepared by dissolving 10 grams of ethyl carbamate and 1 gram of sulfanilamide in a small quantity of hot water and adding enough water to make 100 cubic centimeters. The solution was then sterilized by passing it through a Mandler filter. A few patients were treated with 10 per cent or 20 per cent urethane without sulfanilamide.

An attempt was made to keep the infected wound in contact with the urethane sulfanilamide solution constantly. This was accomplished by wetting the dressing every 4 hours. All wounds were dressed once a day with careful aseptic technique. Cultures were taken and sterile gauze placed within the infected cavity so as to cover all of the crevices. When applying the chemotherapeutic solutions, the dressings were removed only to the inner layer and the drug applied with a sterile syringe in a sufficient quantity to moisten them well. Sterile gauze was then applied, covered with a sterile towel, bandaged, and then covered with waxed paper or oiled silk to prevent evaporation. In cases with sinuses or cavities which could not be saucerized or dependently drained, a perforated catheter or Dakin's tube was inserted, with sterile gauze loosely packed around it. Injections were made through the catheter every 4 hours and the gauze and catheter changed once daily. Whenever wounds were so located as to be frequently contaminated, such as a decubitus ulcer or adjacent to a colostomy, the dressings were changed and saturated with urethane sulfanilamide every time contamination with fecal material occurred.

RESULTS

The effect of urethane sulfanilamide mixture on the gram negative bacteria in infected wounds. Thirty-nine patients were studied and their wound cultures revealed a wide variety of gram positive and gram negative organisms. Staphylococcus aureus, Staphylococcus albus, and Streptococcus pyogenes were by far the most common gram positive bacteria present. Twenty-six of the wounds showed mixed infections yielding both gram positive and gram negative micro-organisms. Fifteen of these re-

vealed the presence of Pseudomonas pyocyanea, 12 Proteus vulgaris, 8 Escherichia coli, and 3 Aerobacter aerogenes. One wound each harbored Bacillus morgani, Klebsiella pneumoniae, and Eberthella typhi. In 6 of the wounds, Proteus vulgaris and Pseudomonas pyocyanea were found together. Only 1 case yielded a pure culture of gram negative bacteria. In 20 (Cases 1 to 20) of the 26 mixed infections, the gram negative members of the wound flora were eradicated with urethane sulfanilamide mixture. Proteus vulgaris and Pseudomonas pyocyanea were found to be most susceptible to the action of the drug mixture, these organisms frequently disappearing from the wounds within 48 to 96 hours. Some of the cases (Cases 4, 5, 13, 16, and 19) showed a slower response but were still classified as good results because elimination of the bacteria was accomplished in spite of such obstacles as fecal contamination, inadequate drainage, etc. The response observed in these wounds appeared to be significantly better than that following the use of other known topical chemotherapeutic agents. Although the wounds in 8 of the individuals (Cases 4, 5, 7, 8, 9, 10, 11, and 20) had a relatively shallow surface affording good contact with the solution, others (Cases 15 and 17) presented situations in which good results were obtained in spite of conditions that were highly unfavorable.

In 7 patients classed as failures, no effect was produced on the gram negative constituents of the wound flora (Cases 21–27). All were in poor general condition, and had either a constant source of wound contamination, inadequate débridement, or insufficient drainage. In addition, 4 of the patients received inadequate treatment with urethane sulfanilamide solution. The infection was classed as chronic in 18 of the patients whose wounds contained gram negative bacteria and as acute in 9 patients. Six of the 7 failures and 12 of the 20 successfully treated infections were classed as chronic; thus, it would seem that the chronicity of the infection as indicated by the duration of the disease and the presence of thick walled granulations and scar tissue was not important in determining the ability of the drugs to eliminate gram negative bacteria from wounds.

Six patients were treated with a solution containing urethane alone (Cases 6, 7, 12, 15, 16, and 21); of these, 5 showed a good response to treatment, with elimination of the gram negative organisms. These results make it seem doubtful that the antibacterial effect of ethyl carbamate is enhanced by sulfanilamide. In 1 patient (Case 4) who had infected ulcers of both lower extremities, a mixture of 10 per cent urethane and 1 per cent sulfanilamide was applied to the lesions on one leg, and a 10 per cent urethane solution alone to those on the other. There was no demonstrable difference in the results. It appeared, therefore, that the urethane was the component in the mixture most active in killing gram negative bacteria, and that the sulfanilamide exerted little, if any, additional effect.

The effect of urethane sulfanilamide mixture on the gram positive bacteria in infected wounds. Gram positive bacteria were present in the wounds of 38 patients. Twenty-six of these showed mixed infections while in 12 only gram positive bacteria were present.

In contrast to the excellent results obtained against gram negative bacteria, urethane sulfanilamide mixture was much less effective against gram positive organisms. Eradication of the gram positive organisms occurred in 12 wounds (Cases 4, 9, 16, 18, 28, 29, 30, 31, 32, 33, 34, and 35), and no effect was demonstrable in 24. In 2 cases (Cases 3, 4) treatment served to eradicate Streptococcus pyogenes from the wound but had no effect on Staphylococcus aureus, while in several other instances the streptococcus was unaffected by the drug. When good results were obtained, the time required for elimination of the bacteria appeared to be considerably longer than that necessary for gram negative organisms. The possibility exists that a similar effect on the gram positive organisms might have been produced by the meticulous use of saline solution, especially in those cases with shallow wounds. Although these bacteria showed only slight susceptibility to urethane, it may have some value in the treatment of infections by decreasing their pathogenicity; in 1 instance, Staphylococcus aureus was noted to change from coagulase positive to coagulase negative and become less actively hemolytic during treatment.

TABLE I.—SUMMARY

Case No.	Age Sex	Diagnosis	Duration of infection	Description of wound	Acute or chronic	General status	Previous chemotherapy	Previous surgery	Treatment		
									Type	Time days	Complications
1	67 F	Milroy's disease	3 weeks	3x3x2 cm. shallow, clean ulcer of leg	Chronic	Fair	Sulfonamide	None	10% ureth. 1% sulf.	15	Vomiting, conjunctivitis
2	23 F	Leg injury 10 years ago. Foreign body removed 2 years ago	2+ years	Ulcer 6x10 cm. right pretibial region—indurated	Chronic	Good	Sulfonamide	Excision of ulcer bed. Three unsuccessful skin grafts. Lumbar sympathectomy. Removal of foreign body	10% ureth. 1% sulf.	10	Vomiting
3	61 F	Arteriosclerotic ulcer, right leg	11 months	11.25x12.5 cm. deep ulcer. Sloughing tendons	Chronic	Poor	?	None	10% ureth. 1% sulf.	9	Nausea
4	73 F	Arteriosclerosis. Leg ulcers, bilateral Carcinoma of sigmoid	9 months	Lower ⅓. Pretibial. Right leg 4.0x5.0 cm. 2x3 cm. Left leg 3.5x4.5 cm. 3.0x2.0 cm.	Chronic	Poor	?	Multiple skin grafts. Femoral ligation, bilateral	Right leg 10% ureth. 1% sulf. Left leg 10% ureth.	23	Nausea and vomiting
5	73 F	Recurrent cancer of breast. Bone metastasis. Diabetes. Decubitus ulcer	5 weeks	Decubitus ulcer over sacrum 10x10x15 cm.	Chronic	Poor	?	Left radical mastectomy 11 months ago	10% ureth. 1% sulf.	7	None
6	M	Varicose ulcers, right leg. Ascending phlebitis. Deep abscess of calf —left	6 weeks	Ulcers at drainage site. Varicose ulcers. 2.5x3 cm. to 3.5x5 cm.	Acute	Good	Sulfonamides Penicillin tyrothrycin locally	Incision and drainage of abscess of calf	10% ureth.	3	None
7	4 M	Second degree burn, right arm	4 months	¾ of surface of right arm involved. Granulating, purulent. Contracture at elbow	Chronic	Good	Sulfonamides penicillin	Several unsuccessful skin grafts	10% ureth.	7	None
8	45 M	Epidermoid carcinoma of nose. Infected wound	2 weeks	Ulcer 0.5 cm. in diam. Purulent base	Acute	Good	None	Excision of carcinoma	10% ureth. 1% sulf.	11	None
9	61 M	Ulcers of left leg	1–2 years	1 ulcer 3x5.5 cm. 1 ulcer 8x6 cm. 1 ulcer 6x4 cm. 1 ulcer 2x2.5 cm.	Chronic	Good	None	None	10% ureth. 1% sulf.	20	None
10	5 M	Second degree burn of upper left arm	2 days	8 cm. in diameter. Purulent base	Acute	Good	None	None	10% ureth. 1% sulf.	10	None
11	9 M	Second degree burn of anterior chest	7 days	Entire left anterior chest wall. Purulent, granulating base	Acute	Fair	None		10% ureth. 1% sulf.	13	None
12	58 M	Cancer of cecum	7 days	Postoperative wound infection. Wound opened down to the fascia	Acute	Fair	Sulfonamides (current)	Resection of cecum. Ileotransverse colostomy	20% ureth.	4	None
13	72 F	Strangulated femoral hernia, postoperative	10 days	20 cm. inguinofemoral incision. Sloughing fascia. Open only for 4 cm. at one end. Draining thick pus	Acute	Poor	Sulfonamides	Repair of strangulated femoral hernia	10% ureth. 1% sulf.	10	Nausea and vomiting

OF CASES

Cultures of wounds		Adequate surgical treatment	Adequate urethane treatment	Clinical result	Bacteriological result	Remarks
Before treatment	After treatment					
Staphylococcus aureus Ps. pyocyanea	Present Absent Staphylococcus albus Diphtheroids	Yes	Yes		Excellent gram negative Poor gram positive	Ps. pyocyanea disappeared in 48 hours
Proteus vulgaris Ps. pyocyanea Esch. coli Staphylococci Streptococcus pyogenes	Absent Absent Absent Present Present	Yes	Yes	Grafted in stages. Condition good 21 months later	Excellent gram negative Poor gram positive	Gram negative organisms disappeared in 96 hours
Diphtheroids Ps. pyocyanea Streptococcus pyogenes Staphylococcus aureus	Absent Absent Absent Present	Yes	Yes		Excellent gram negative Fair gram positive	Ps. pyocyanea disappeared in 72 hours
Proteus vulgaris Staphylococcus aureus Streptococcus pyogenes	Absent Present Absent	Yes	Yes	Excellent	Excellent gram negative Fair gram positive	Ulcers grafted, 100% take. Proteus gone in 5 days. No difference in results of urethane sulfanilamide combination and urethane alone
Proteus vulgaris Ps. pyocyanea Staphylococcus aureus Staphylococcus albus Streptococcus pyogenes	Absent Absent Present Present Present	Yes	Yes		Excellent gram negative Poor gram positive	Gram negative organisms disappeared in spite of fecal contamination. Ps. pyocyanea gone in 48 hours, proteus in 7 days
Ps. pyocyanea Streptococcus pyogenes Hemolytic Staphylococcus aureus	Absent Present Present	Yes	Yes	Good (healed)	Excellent gram negative Poor gram positive	Treated with urethane for 3 days because of a gram negative contaminant. Ps. pyocyanea disappeared in 72 hours
Hemolytic Staphylococcus aureus Streptococcus pyogenes Diphtheroids B. morgani B. mucosus capsulatus	Present Present Absent Rare Absent	Yes	Yes	Good. Grafted in stages	Good gram negative Poor gram positive	
Proteus vulgaris Staphylococcus albus	Absent Present	Yes	Yes	Excellent	Excellent gram negative Poor gram positive	Proteus disappeared after 48 hours of treatment. Nose graft—80% take
Staphylococcus albus Ps. pyocyanea A. aerogenes	Absent Absent Absent		Yes	Excellent	Excellent gram negative Excellent gram positive	All ulcers healed. Largest grafted. Grafts took in presence of constant urethane soaks
Staphylococcus albus Esch. coli Proteus vulgaris	Present Absent Absent		Yes	Excellent	Excellent gram negative Poor gram positive	Gram negative organisms gone after 48 hours of treatment. Never returned. Complete healing in 3 weeks
Staphylococcus albus Proteus vulgaris Ps. pyocyanea	Present Absent Absent		Yes	Excellent	Excellent gram negative Poor gram positive	Gram negative bacteria permanently gone after 4 days of treatment. Successfully grafted
Esch. coli Nonhemolytic streptococcus	Absent Present Streptococcus viridans	Yes	Yes	Alive and well 2 years postoperatively. Wound firm, well healed	Excellent gram negative Poor gram positive	Wound sutured after 4 days of treatment. Prompt healing
Proteus vulgaris Esch. coli Staphylococcus aureus	Absent Absent Present	No	Fair		Excellent gram negative Poor gram positive	Patient uncooperative. Wound should have been opened widely. Proteus gone in 4 days

TABLE I.—SUMMARY

Case No.	Age Sex	Diagnosis	Duration of infection	Description of wound	Acute or chronic	General status	Previous chemotherapy	Previous surgery	Treatment		
									Type	Time days	Complications
14	38 M	Infected postoperative nephrectomy wound. Sinus to kidney bed	2 months	Multiple sinus tracts scar to kidney bed. Demonstrated by lipiodol	Chronic	Good	?	Nephrectomy	10% ureth. 1% sulf.	30	Nausea
15	50 M	Infected nephrectomy wound. Sinuses to kidney bed	3 months	Multiple sinuses to kidney bed from unhealed, discharging nephrectomy wound	Chronic	Poor	?	Nephrectomy	10% ureth.	43	Nausea and vomiting
16	53 F	Osteochondritis of hips, bilateral. Decubitus ulcer	10 days	Decubitus ulcer over sacrum. 10 cm. diam. abscess of buttocks	Chronic	Poor	Urea sulfathiazole ointment	Hip manipulation	10% ureth.	31	Nausea and vomiting
17	17 F	Multiple sinuses of arm and shoulder	3 years	Multiple deep sinus tracts about shoulder girdle	Chronic	Fair	Sulfanilamide gramicidin penicillin	Multiple excision of sinus tracts	10% ureth. 1% sulf.	24	None
18	M	Chronic empyema, right	1½ years	Draining cavity, right	Chronic	Good	Sulfonamide	Rib section	10% ureth. 1% sulf.	2	Nausea and vomiting
19	55 M	Cancer of cecum. Extensive wound infection	2 weeks	Wound opened widely down to fascia	Acute	Good	Urea solution for 2 weeks	Right colectomy	10% ureth. 1% sulf.	8	None
20	45 M	Arteriosclerotic ulcer at base of great toe, right	2 days	Ulcer with draining sinus at base of toe	Acute	Fair	None	None	10% ureth. 1% sulf.	4	None
21	66 F	Diabetes mellitus. Sloughing ulcer of foot, postoperative	1 month	Tremendous sloughing undermining postoperative ulcer of dorsum of foot and lower leg	Chronic	Very poor	Sulfonamide	Amputation of a toe	20% ureth.	10	Retching
22	Elderly F	?G.I. malignancy. Decubitus ulcer		Intergluteal fold undermining decubitus ulcer, with sinuses and sloughing fascia 10x6x10 cm.	Chronic	Poor	?	None	10% ureth. 1% sulf.	5	None
23	58 M	Carcinoma of sigmoid with perforation. Left groin abscess draining spontaneously		Large, granulating wound left groin with sinuses, discharging thick pus. Induration to costal margin. Crepitus to neck	Chronic	Poor		Cecostomy and transverse colostomy, both functioning	10% ureth. 1% sulf.	8	None
24	27 M	Ulcerative colitis with hemorrhage. Perirectal abscess	3 months	Perirectal cavity 6x5x6 cm. draining purulent material	Chronic	Poor	None	Ileostomy. Drainage of rectal abscess	10% ureth. 1% sulf.	3	None
25	65 F	Hodgkin's disease. Postradiation slough in neck	4 months	Foul necrotic sloughing crater in neck extending into mediastinum. Multiple sinuses. No dependent drainage	Chronic	Very poor	Sulfonamide Zinc peroxide Azochloramide Urea crystals	Biopsy of neck lymph node	10% ureth. 1% sulf.	10	Nausea and vomiting
26	17	Chronic empyema	20 months	Tube strapped into a small sinus in chest	Chronic	Fair	?	Thoracotomy elsewhere	10% ureth. 1% sulf.	14	Vomiting (see remarks)

OF CASES—Continued

Cultures of wounds		Adequate surgical treatment	Adequate urethane treatment	Clinical result	Bacteriological result	Remarks
Before treatment	After treatment					
Proteus vulgaris Staphylococcus aureus Ps. pyocyanea Diphtheroids	Absent Present Absent Absent	Yes wide open drainage	Yes	Excellent (cure)	Excellent gram negative Poor gram positive	Proteus and Ps. pyocyanea rare after 90 hours; gone after 16 days. Excellent result demonstrating the use of chemotherapy in conjunction with adequate surgery
K. pneumoniae Staphylococcus aureus Staphylococcus albus Diphtheroids Ps. pyocyanea Proteus vulgaris	Absent Present Absent Present Absent Absent Streptococcus pyogenes	No	Yes	Wound improved clinically	Good gram negative Poor gram positive	Good gram negative result in spite of inadequate drainage. Proteus absent in 23 days. Ps. pyocyanea rare colony after 23 days
Ps. pyocyanea Nonhemolytic streptococcus Nonhemolytic Staphylococcus aureus Diphtheroids	Absent Absent Absent Absent	Yes	Yes	Excellent. Ulcer sterilized. Grafted —100% take	Excellent gram negative Excellent gram positive	Ps. pyocyanea gone after 23 days. Easily contaminated area
Hemolytic Staphylococcus aureus Esch. coli	Present Absent	No	No	Poor	Excellent gram negative Poor gram positive	Disappearance of coli 48 hours after treatment
Ps. pyocyanea Staphylococcus albus	Absent Present	No	Yes	Good	Excellent gram negative Excellent gram positive	Ps. pyocyanea gone 48 hours after treatment started. No recurrence
Esch. coli	Absent	Yes	Yes	Excellent	Excellent gram negative	Wound sterile after 5 days of treatment. Wound edges pulled together with adhesive tape. Complete healing
Ps. pyocyanea Streptococcus pyogenes	Absent Present	No	No	Poor	Excellent gram negative Poor gram positive	Leg amputated on 4th day. Ps. pyocyanea gone after 48 hours of treatment
Staphylococcus aureus Proteus vulgaris Diphtheroids	Present Present Present Esch. coli Streptococcus pyogenes	No	Yes	Patient died	Poor gram negative Poor gram positive	Hopeless case. No adequate surgical drainage
Proteus vulgaris Ps. pyocyanea Esch. coli Staphylococcus Diphtheroids	Present Present Present Present Present	No	Yes		Poor gram negative Poor gram positive	Abandoned because of lack of surgical control (ulcer needed débridement) and constant fecal contamination. Not a fair test
Cl. welchii Esch. coli Ps. pyocyanea	Present Present Present Staphylococcus aureus	No	Yes		Poor gram negative Poor gram positive	Not a fair test. Abandoned due to constant fecal contamination
Gram negative bacilli—type undetermined	Present	No	No	Eventually good	Poor gram negative Poor gram positive	Abandoned because of fecal contamination. Not a fair test
Proteus vulgaris Ps. pyocyanea Streptococcus pyogenes	Present Present Present Staphylococcus	No	No	Poor	Poor gram negative Poor gram positive	Unfaithful treatment. No dependent drainage. Multiple sinuses
Staphylococcus aureus Ps. pyocyanea Streptococcus pyogenes	Present Present Present	No	No		Poor gram negative Poor gram positive	Adequate treatment impossible because of vomiting. This probably not due to urethane because it only occurred during irrigations

TABLE I.—SUMMARY

Case No.	Age Sex	Diagnosis	Duration of infection	Description of wound	Acute or chronic	General status	Previous chemotherapy	Previous surgery	Treatment		
									Type	Time days	Complications
27	40 M	Staphylococcal empyema secondarily infected with Esch. coli	2 months 1 day of secondary infection	Foul, gray, thin pus draining from opening in chest	Acute	Poor	Pencillin	Rib resection	10% ureth. 1% sulf.	9	None
28	41 F	Obesity ++. Twisted ovarian cyst	7 days	Postoperative wound separation down to fascia. Adipose tissue 5 inches deep with fat liquefaction	Acute	Good. Except obesity	Sulfonamides current)	Excision twisted ovarian cyst, left	10% ureth. 1% sulf.	7	None
29	42 M	Wound infection (ventral hernia). Chronic empyema. Cardiac decompensation	27 days	Massive infection of ventral herniorrhaphy wound. Fascia not involved	Acute	Poor	Sulfonamides Activated zinc peroxide Dakin's solution	Drainage of empyema. Repair of ventral hernia	10% ureth. 1% sulf.	7	None
30	70 M	Decubitus ulcer and gluteal abscess	2 weeks	Large crater-like wound involving whole left buttock. Purulent base	Acute	Good	Urea solution	Incision and drainage of gluteal abscess. Midthigh amputation, left	10% ureth. 1% sulf.	50	None
31	47 F	Varicose ulcer of left lower leg	1½ years	5.5x3.0 cm. ulcer. Purulent base. Extensive epidermophytosis	Chronic	Good	Various topical medications	None	10% ureth. 1% sulf.	18	None
32	65 M	Acute cellulitis of left leg	4 days	Two sinuses leading into area of cellulitis. Cavity under skin 3x3 in.	Acute	Fair	Sulfadiazine	Incision and drainage of subcutaneous abscess	10% ureth. 1% sulf.	30	None
33	F	Ulcer of left leg, 2 years' duration	About 1 week	Ulcer 2 cm. in diam. Recent sloughing of skin grafts. Purulent exudate	Chronic	Good	None	Skin graft	10% ureth. 1% sulf.	13	None
34	55 F	Burn of scalp, infected. Gumma of scalp	3 weeks	Burn 2 cm. in diameter. Bone exposed. Purulent	Acute	Good Patient had tertiary lues	None	None	10% ureth. 1% sulf.	35	None
35	60 F	Multiple ulcers of legs. Varicose veins	2 years	Twenty-nine ulcers about ¼–½ cm. in diam. on both lower legs. Undermining. Purulent base	Chronic	Good	None	None	10% ureth. 10% sulf.	16	None
36	57 M	Epidermoid carcinoma of left foot and groin	13 days	10x2.5x1.5 cm. wound in groin. Postoperative slough	Chronic	Poor	None	Left thigh amputation. Left groin dissection	10% ureth.	6	None
37	25 M	Osteomyelitis of pelvis	3–4 days	Ulcer 2 cm. in diam. over left iliac crest with sinus holding 4.0 c.c.	Chronic	Good	Penicillin	Drainage osteomyelitis	10% ureth. 1% sulf.	6	None
38*	68 F	Typhoid wound infection—postoperative. Fracture of femur	17 days	Sinus in center of scar. Draining thin, gray, foul pus. Cavity held 30 c.c.	Acute	Fair	None	Open reduction of fracture of femur with insertion of Blount pin	10% ureth. 1% sulf.	12	None
39	Abt. 50 F	Amputation of leg with infection of stump	About 2 weeks	Amputation stump covered with thick yellow pus—edges widely separated	Acute	Good		Amputation of leg	10% ureth. 1% sulf.	34	None

*This case has been reported in detail by one of us (L. W.) in the *N. England J. M.*, 1946, 234: 184–187.

OF CASES—Continued

Cultures of wounds		Adequate surgical treatment	Adequate urethane treatment	Clinical result	Bacteriological result	Remarks
Before treatment	After treatment					
Esch. coli Staphylococcus aureus	Present Present	No	?	Poor	Poor gram negative Poor gram positive	Urethane instilled into pleural cavity 2–4 times a day
Streptococcus pyogenes Nonhemolytic streptococcus Staphylococcus aureus	Present Present Absent	Yes	Yes	Slow wound healing due to fat liquefaction	Fair gram positive	Staphylococcus aureus disappeared in 96 hours
Hemolytic Staphylococcus aureus Nonhemolytic Staphylococcus aureus Alpha streptococci Nonhemolytic streptococcus Cl. welchii Diphtheroids Staphylococcus albus	Absent Absent Present Absent Absent Absent Absent	Yes	Yes	Good (healed)	Good gram positive	
Staphylococcus aureus hemolytic, coagulase positive	Organisms less hemolytic and coagulase negative	Yes	Yes	Excellent. Wound completely healed	Fair gram positive	Sterilization not accomplished
Hemolytic Staphylococcus aureus Diphtheroids	Absent Absent		Yes	Complete healing of ulcer	Excellent gram positive	Exudate disappeared from ulcer 24 hours after start of treatment, and healing began shortly
Streptococcus pyogenes	Absent	Yes	Yes	Excellent	Excellent gram positive	Wound sterilized in 8 days of treatment. Sterility maintained
Hemolytic Staphylococcus aureus—coagulase positive	Absent	Yes	Yes	Excellent	Excellent gram positive	Wound completely sterile in 3 days of treatment and healed in 14 days
Hemolytic Staphylococcus aureus	Absent		Yes	Good	Good gram positive	Wound reduced to ½ original size by treatment. Patient then started on antiluetic treatment
Anaerobic streptococcus	Absent	Yes	Yes	Excellent	Excellent gram positive	Wounds completely sterile after 48 hours of treatment. Completely healed after 16 days
Staphylococcus aureus B. subtilis	Present Absent Esch. coli Diphtheroids	Yes	Yes	Died of pulmonary metastasis	Poor gram positive	Treatment stopped at request of his physician after 6 days Inadequate trial
A. aerogenes Staphylococcus aureus	Absent Present		Yes	Excellent	Excellent gram negative Poor gram positive	Sinus and ulcer completely healed in a week
B. typhi	Absent		Yes	Excellent	Excellent. E. typhi	Wound sterile after 48 hours of treatment. Sinus decreased rapidly in size and was completely closed 15 days after start of urethane treatment
Hemolytic Staphylococcus aureus coagulase positive	Present	Yes	Yes	Very good	Poor gram positive	Wound almost completely healed at the time patient was sent home after 34 days of treatment

Of the 12 wounds in which elimination of gram positive bacteria was produced, the infections in 7 were classified as chronic and in 5 as acute. Nine of the patients were in fair or good general condition, and the clinical status of 3 was poor. Five of the patients in whom good results were obtained had had previous sulfonamide therapy, and all except 1 were subsequently treated with a mixture of 10 per cent urethane and 1 per cent sulfanilamide.

Analysis of the 26 failures to eliminate gram positive bacteria from wounds by the use of urethane sulfanilamide solution showed that in 13 there were such obvious reasons as inadequate drainage, constant fecal contamination, etc.

It should be stressed that, of the 26 cases of mixed infections in which treatment failed to eradicate the gram positive bacteria, 15 (Cases 1, 2, 3, 5, 6, 7, 8, 10, 11, 12, 13, 14, 15, 17, and 20) showed complete elimination of the gram negative organisms, while in none of the 7 gram negative failures were the gram positive organisms in the same wound eradicated. These cases show the highly selective action of urethane dependent on the staining reaction of bacteria.

Complications. Careful observation failed to reveal a hypnotic effect in any of the 39 patients treated by the topical application of urethane. One patient was given 10 grams of urethane orally in 24 hours without untoward reaction. Nine of the topically treated individuals suffered from nausea and vomiting, 2 from nausea alone, and 1 from retching. These symptoms were at times severe enough to cause moderate discomfort and were sufficiently alarming to warrant discontinuation of the drug in 1 instance (Case 26). In this patient, psychogenic factors were thought to play a large part. The nausea usually began after 3 or 4 days of treatment, reached a peak on the fifth or sixth day, and then decreased, to continue moderately thereafter. The 12 patients who showed these symptoms were treated for an average of 19 days, the shortest being 9 days and the longest 43 days. Seven of those who had gastrointestinal symptoms had previously received some type of sulfonamide; in the remaining 5 patients no information concerning the previous use of these drugs was available. That the nausea and vomiting were not due to sulfonamide sensitivity was borne out by the fact that they occurred in 3 individuals who were treated with urethane solution alone. The wounds in 10 of the 12 patients who had gastrointestinal disturbances were relatively large, and it was our impression that the symptoms occurred more frequently when large surface areas of normal surrounding skin were kept constantly moist with urethane solution. This suggested that the drug was absorbed through normal skin, and other observations tended to bear out this theory. One patient, not included in this study, who had severe pyodermia over the entire thorax and trunk and was treated with a large amount of urethane suffered very severe nausea and vomiting. During the latter part of the investigation, therefore, the normal skin was covered with vaseline gauze up to the wound edge in order to prevent absorption. With this type of management, no other instances of nausea or vomiting were seen.

SUMMARY AND DISCUSSION

Meleney (16) has called attention to the difficulty of appraising the value of drugs used for the treatment of surgical infections and has enumerated many factors which must be taken into consideration in evaluating their efficiency. In certain acute surgical infections, a series of unselected alternate patients with relatively few variables can be treated under standard conditions, and the value of a chemotherapeutic agent assessed quite correctly. In the cases reported here in which most of the wounds were chronic, occurred in patients with a wide variety of underlying conditions, and included some which had been previously treated by various methods, it is difficult to assess the value of an antibacterial agent because of the lack of adequate controls. It is necessary, therefore, to use the patient's previous response to other types of therapy as a control and to stress the importance of changes in the bacterial flora. In order to conclude that ethyl carbamate is of value, the results obtained must be significantly better than those expected after other types of treatment.

As can be seen from the data presented, urethane has a selective action against gram

negative organisms. These results are in accord with those previously described in *in vitro* studies. The reason for this selectivity is not known, but it would appear to be of great value in the treatment of wounds with mixed infections since, with the exception of streptomycin, there are few agents which are highly active against gram negative organisms.

Most of the patients in this study were treated with a combination of sulfanilamide and urethane. Several cases given carbamate alone appeared to show as good a response as those receiving a combination of the drugs, and it is our impression that the addition of sulfanilamide may not be necessary. *In vitro* studies of ethyl carbamate separately and in combination with sulfonamide yielded the same results, although a slight synergistic effect could be demonstrated when the two drugs were combined. It has been shown by Weinstein that penicillin plus urethane will inhibit greatly the growth of mixtures of gram positive and gram negative bacteria in the test tube. These data suggest the possibility of using a mixture of urethane and penicillin in the treatment of wounds. With such a combination, the gram positive organisms should be killed by the penicillin and the gram negative organisms by the carbamate. An agent potently bactericidal for the gram negative group should prevent or limit their production of substances, such as penicillinase (1), which inhibit the action of penicillin, and should thus render the latter more efficacious.

Urethane showed no deleterious effect on tissue healing, since large wounds were found to heal promptly after being sterilized. Skin grafts took successfully when postoperative dressings were kept continuously saturated with urethane (Cases 4, 9, 11, and 8). Epithelization was observed to progress at a normal rate in the constant presence of 10 per cent urethane solution.

The complications seen in patients receiving urethane have already been described. Nettleship, Henshaw, and Meyer have called attention to the carcinogenic effect of ethyl carbamate in mice. These investigators increased the incidence of lung tumors in C_3H female mice[1] from less than 5 per cent to more than 75 per cent by minimal, anesthetizing, intraperitoneal injections of urethane, by a dose of 1 milliliter of a 10 per cent aqueous solution per 100 grams of body weight. Haddow and Sexton (5), on the other hand, have shown that urethane has a growth-inhibiting effect on animal tumors, and Paterson, Haddow, Thomas, and Watkinson (19) have recently reported beneficial effects from the use of urethane in myeloid and lymphoid leucemia, carcinoma of the breast, lymphosarcoma, Hodgkin's disease, and other malignant lesions.

In some of the cases reported in the present study, the quantity of urethane used probably exceeded the level used by Nettleship and coworkers, but it was employed as a topical agent and was not administered parenterally. Although some was undoubtedly absorbed through the skin or wound, it does not appear likely that the amount was as great per unit of body weight as that given intraperitoneally to mice by Nettleship and his coworkers. There would appear to be little to fear regarding the carcinogenic effect of urethane in man. The fact that the incidence of tumors in a known tumor susceptible strain of mice is increased by the administration of some substance does not mean that such a result would follow the use of the same material in man; for example, the administration of estrogenic substances is known to enhance the occurrence of breast tumors in mice, yet these agents have been used very extensively in women.

Although urethane has been shown to be very effective against gram negative organisms and to allow normal wound healing, it must be remembered that the use of this or any other drug does not replace the application of sound surgical principles. Experience in World War II (2, 12, 28) has demonstrated that the presence or absence of bacteria is not important in choosing the proper time for suture of soft tissue wounds, failure having followed the closure of clinically dirty wounds which were sterile, and success having resulted after suture of wounds massively contaminated with staphylococci and streptococci. It is not reasonable to expect the eradication of bacteria to result from the topical application of a chemotherapeutic agent to wounds in which the

[1] An inbred strain of mice with a high incidence of mammary cancer.

organisms are harbored in deep sinuses or crevices, or are contained in sealed lymphatics impermeable to the drug. There are many instances in which scar tissue, necrotic tissue, and poor blood supply prevent even a most potent chemotherapeutic agent, administered either systemically or topically, from reaching an infected area in sufficient concentration to exert its bacteriostatic or bactericidal effects. The removal of necrotic tissue and the institution of adequate drainage, are most important in the treatment of infected wounds and without these even the most active chemotherapeutic agent may fail.

CONCLUSIONS

1. Urethane appears to be an effective agent for the elimination of gram negative bacteria from mixed wound infections.

2. The activity of urethane against gram positive bacteria in infected wounds is minimal.

3. Wound healing in man does not appear to be inhibited by the use of urethane.

4. Gastrointestinal symptoms may result from the topical application of urethane but appear to be of little significance.

5. Investigation of the action of urethane penicillin mixtures in the treatment of mixed surgical wound infections is indicated.

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GELATIN SOLUTION IN THE TREATMENT OF SHOCK FROM GRADED HEMORRHAGE

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THE marked individual variability of resistance and recuperative power of the dog to procedures for the production of shock has been a serious handicap in obtaining clear-cut results with various forms of shock therapy. Experimental technique and conditions can be standardized, but the biologic variability of the animal cannot be made uniform. Unless the difference in effectiveness of the agents tested is very striking, as between blood or plasma and saline, large numbers of animals will be required to overcome the variability of the individual animal.

Rather than employing large numbers, we attempted to classify the experimental animal with regard to its ability to resist to, and to recover from, shock by graded bleeding. A study (1) on dogs subjected to hourly bleedings of 25, 23, 21, 19, and 17 per cent of the original measured blood volume, and reinfused ½ hour after each bleeding with all but 2 per cent of the withdrawn blood, that is, 23, 21, 19, 17, and 15 per cent, led to the following conclusions:

1. The initial bleeding of 25 per cent of the calculated blood volume and the succeeding half hour oligemic interval constituted a "provocative test" of shock resistance.

2. The arterial plasma carbon dioxide content ½ hour after a hemorrhage of 25 per cent of the total blood volume is a reliable index of the resistance and recuperative powers of most of the animals and also a reliable means of predicting the likelihood of recovery from the subsequent experimental procedure.

3. The product of maximal blood pressure and arterial carbon dioxide content ½ hour after the initial hemorrhage correlates as clearly with the subsequent survival of animals as does the carbon dioxide value and seems to have an advantage in some instances over the carbon dioxide value alone, although both have equal statistical significance. This product of maximal blood pressure and arterial carbon dioxide content has been designated the "factor of probability of survival." In this study, we found that dogs with a low factor of probability of survival (below 1,000) or a low carbon dioxide value (10–20 volumes per cent) did not survive the procedure of 5 graded hemorrhages alternated with 5 reinfusions of their blood. With a medium factor of probability of survival (1,700–3,000) or a medium carbon dioxide value (20–30 volumes per cent) about half of the animals survived more than 24 hours. With a high factor of probability of survival (over 3,000) or a high carbon dioxide value (over 30 volumes per cent) all animals survived indefinitely.

Since the carbon dioxide value and factor of probability of survival, after a "provocative test" of hemorrhage, provide a means of classifying the experimental animal and predicting the probable outcome, we believed that small series of experiments of 10 animals with medium factor of probability of survival and carbon dioxide values could provide reliable information on the relative value of different agents to be tested for their shock-combatting properties.

There are many reports extant on the efficacy of gelatin for this purpose, and we have had favorable results with infusions of gelatin in dogs (17) and in man (18). It has been well established that, if proper precautions are taken, pyrogen-free solutions of gelatin can be prepared. Such solutions cause no untoward reactions and are not sensitizing in nature. The relative values of different concentrations of gelatin and of so-called "high plunge" or "low

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TABLE I

Our lab. No.	Obtained from	Origin	Per cent concentration	Plunge*	Condition at room temperature
A	Wilson & Co.	Pigskin	8	Medium and high (60–100)	Liquid
B	Wilson & Co.	Pigskin	8	Low (30–60)	Liquid
C	Wilson & Co.	Pigskin	4	High & low (28–117)	Liquid
D	Wilson & Co.	Pigskin	2	High (18–37)	Liquid
E	Atlantic	Pigskin	7	Medium (80)	Liquid
F	Atlantic	Pigskin	¾	Medium (80)	Liquid
G	Knox	Bone	6	High (131)	Solid

*The "plunge" of gelatin is an expression of its gel strength and is determined by the weight required to make a stylus penetrate a given depth at 4°C.

plunge" gelatin, i.e., slightly degraded or markedly degraded material, have not been well established. This study was undertaken, therefore, from the viewpoint of comparing the efficacy of different concentrations of gelatin and of gelatins of varying degrees of hydrolysis.

In Table I are listed the variety of gelatins tested and some of the pertinent information obtained.

We attempted to use animals with a medium factor of probability of survival (1,700–3,000) and with medium carbon dioxide (20–30 volumes per cent) value, except when 2 per cent gelatin and saline were employed. With the latter two materials, we purposely chose animals with a high factor of probability of survival and a high carbon dioxide value, because it became clear, very early, that these substances were relatively ineffective.

Methods. The experimental procedure and methods used were those described previously (1), with one exception: after the hemorrhage, the blood was quickly centrifuged, the supernatant plasma removed and, at the reinfusion, a volume of test material equal to the removed plasma was injected, followed by the packed red blood cells. There could not be complete substitution of the test material for the plasma, for about 6 per cent of the latter was retained around the packed red blood cells and reinfused with them. This was constant, however, for the varying substances tested. Blood pressures were recorded continually from a carotid artery. One femoral artery was used for bleeding and for withdrawal of blood samples for analysis. All surgical procedures were performed on dogs under local anesthesia (procaine).

RESULTS

Antishock properties and survival. The efficacy of the gelatin was based on the period of survival of the animal. In the tables, D. E. signifies death occurring during the experiment, D. N. indicates longer survival but death during the night following the experiment, and I. S. means indefinite survival, in which group we placed all animals alive 48 hours after the experiment. Rarely did an animal fail to survive indefinitely if it was still alive 24 hours after the experiment. Table II presents a summary of all experiments. The data previously obtained (1) when whole blood was reinfused are included for comparison at the bottom of the table. The results presented in this table lead to several clear-cut conclusions.

1. Confirming the previously expressed results, most animals with a carbon dioxide value less than 20 volumes per cent and a factor of probability of survival under 1,700 will not survive regardless of the reinfusing fluid, even when whole blood, presumably the best, is used.

2. Animals with a carbon dioxide value above 30 volumes per cent and a factor of probability of survival above 3,000 have a good prospect of survival if the reinfusing agent has definite restorative properties.

3. On the basis of our criteria, saline has the least value in saving animals.

4. Two per cent gelatin is only little better than saline.

5. Four per cent gelatin has definite value, is strikingly better than saline, but is somewhat inferior to gelatin of higher concentrations.

6. Gelatin of 6 to 8 per cent concentration is a very effective agent. The relative merits of the different concentrations and plunges are not so clearcut. Statistical analysis of the results, by the chi square test, discloses that there is no overall difference between blood and gelatin, and, in general, all the higher concentration gelatins are equivalent. Statistical

TABLE II.—SUMMARY OF AVERAGE VALUES AND RESULTS

Average CO_2 volume per cent	Average B. P. mm. Hg.	Average F. P. S.	No. of dogs	Survival*						Average hours survival of dogs that died
				D. E.		D. N.		I. S.		
				No.	Per cent	No.	Per cent	No.	Per cent	
				Gelatin A (8%)						
8.3–19.9	78	1199	8	5	62	3	38	0	0	7.0
20 –24.9	74	1683	8	4	50	4	50	0	0	10.0
25 –29.9	77	2132	8	0	0	4	50	4	50	19.6
30 –40	100	3379	7	0	0	3	43	4	57	13.0
				Gelatin B (8%)						
16.2–19.9	62	1128	3	3	100	0	0	0	0	2.5
24.2–29.9	77	2096	5	0	0	3	60	2	40	10.8
30 –39.9	88	3031	10	1	10	5	50	4	40	12.8
				Gelatin C (4%)						
15 –19.9	70	1197	5	[illegible]	80	1	20	0	0	3.8
20 –24.9	80	1717	7	7	86	1	14	0	0	4.2
25 –29.9	70	1999	9	3	33	2	22	4	45	4.6
30 –40.2	72	2568	4	1	25	1	25	2	50	6.3
				Gelatin D (2%)						
25 –29.9	96	2593	5	5	100	0	0	0	0	3.4
30 –40.3	99	3496	8	6	74	1	13	1	13	6.3
				Gelatin D (7%)						
9.6–14.9	50	560	2	2	100	0	0	0	0	1.0
20 –24.9	66	1483	5	3	60	1	20	1	20	6.2
25 –29.9	98	2681	5	0	0	1	20	4	80	13.0
35 –39.9	118	4218	3	0	0	0	0	3	100	....
				Gelatin E (7%)						
7.6–19.9	63	900	4	3	75	1	25	0	0	5.1
25 –29.9	70	1920	5	0	0	4	80	1	20	13.0
30 –40.5	97	3486	3	0	0	0	0	3	100	....
				Gelatin G (6%)						
17.8–17.9	82	1463	2	2	100	0	0	0	0	2.5
20 –24.9	81	1774	3	3	100	0	0	0	0	3.5
25 –32	94	2611	7	0	0	4	57	3	43	13.0
				Saline						
22.9–23.3	98	2273	2	2	100	0	0	0	0	2.0
25 –29.9	94	2585	4	4	100	0	0	0	0	3.7
35 –42.0	119	4566	4	4	100	0	0	0	0	2.8
				Whole blood						
11.3–19.9	83	1237	10	10	100	0	0	0	0	2.4
20 –24.9	75	1618	10	5	50	2	20	3	30	6.0
25 –29.9	78	2104	9	2	22	3	33	4	45	8.0
30 –42.6	81	2838	12	1	8	3	25	8	67	9.7

F. P. S.—Factor of probability of survival.
*D. E. signifies death occurring during the experiment; D. N. during the night; and I. S. indefinite survival.

TABLE III.—RESULTS OF GELATIN REINFUSION IN DOGS SUBJECTED TO GRADED HEMORRHAGE, WHOSE CARBON DIOXIDE VALUES AFTER FIRST INFUSION WERE BETWEEN 20 AND 30

Gelatin	No. dogs	Average CO^2	Survival in per cent		
			DE*	DN	IS
A & B (8%)	20	25.3	20	55	25
C (4%)	15	24.4	56	19	25
E & F (7%)	15	25.5	20	40	40
G (6%)	9	25.3	33	55	12

*See footnote Table II.

differences are only suggestive, but inconclusive. The relative evaluation of the different gelatins, therefore, rests on other considerations. In our experience, we could observe no definite differences in the antishock properties or survival effects of so-called "high plunge" and "low plunge" gelatins. The important property was the concentration of gelatin which should be 6 per cent or higher, to give the best effect. Gelatin was obtained from three different sources (Atlantic, Knox, and Wilson). In Table III are presented the results for the critical testing range where carbon dioxide values fell between 20 and 30, a zone which we have felt might be critical for distinguishing finer differences in the merit of different antishock agents. Although there are no statistically significant differences, it appears that:

1. The 4 per cent pigskin gelatin does not have as good immediate shock-combatting efficacy.

2. The 6 per cent bone gelatin does not have as good survival effect.

In general, the clinical condition of the animals during the experiment and afterward supported these inferences. The results with the 6 per cent bone gelatin were slightly surprising. Because of the good initial effect from this material, we expected more animals would survive indefinitely. Two animals, which survived through the first 24 hours, died in the following 24 hours. This was unusual, for in our experience if animals survived through the first night, they rarely failed to survive indefinitely. We cannot account for this delayed death but at autopsy, in addition to the findings of pulmonary congestion and edema which was appreciably observed in animals which failed to survive the experimental procedure, we also noted in one animal a markedly enlarged liver of gelatinous appearance, while in the second the spleen was about twice normal size and also gelatinous in appearance; relatively large amounts of gelatinous material could be expressed from both organs. This does not explain the delayed deaths, but it may indicate that the 6 per cent bone gelatin had accumulated in these organs. From the survival viewpoint, the 7 per cent pigskin gelatin seemed best. This was particularly true of the first lot which we tested and which, although slightly pyrogenic, was probably the best material we used, both from an immediate shock-combatting effect as well as ultimate survival. We cannot account for the apparent superiority of this particular lot of gelatin, because we have no information of its method of manufacture and properties other than its concentration and plunge.

TABLE IV.—BLOOD GELATIN CONCENTRATION (GMS. %)

Gelatin code No. and concentration	After 5th infusion	24 hrs. later
A*—8%	2.49	0.48
B —8%	2.37	0.54
C —4%	1.18	0.25
E —7%	2.22	0.56
F— 7%	1.79	0.41
G —6%	2.87	1.15

*A–F is skin gelatin; G is bone gelatin.

Secondary findings.

1. Elimination rate of gelatin: Table IV presents the average values of the concentration of gelatin in the blood. Since the proportion of infused gelatin was approximately the same, and since massive amounts were infused, these values indicate the rate of elimination or, conversely, the retention of the gelatin in the blood stream. There appears to be no great difference in the rate of excretion of gelatins, regardless of plunge or concentration, except for G, the 6 per cent bone gelatin. This product showed a much greater property of remaining in the blood stream. With all the other gelatin preparations, there was only a

negligible amount left after 24 hours, despite the massive infusion. In contrast to this, the 6 per cent bone gelatin was still present after 24 hours in more than twice the quantity of any other preparation. In fact, after 24 hours, there was as much gelatin in the blood stream from infusion of 6 per cent bone gelatin as there was at the end of the last infusion of 4 per cent pigskin gelatin. It may be concluded from the rate of elimination that the other forms of gelatin, regardless of plunge, are eliminated rather rapidly and therefore can have only a temporary effect, whereas the bone gelatin which had the least hydrolysis and was solid at room temperatures, should have a more prolonged action; the latter point will be discussed below.

2. Blood and plasma volume: The changes in the whole blood and plasma volumes determined at the end of the experiment and 24 hours later are presented in Table V. The animals which received 4 per cent and 7 per cent gelatins showed a definite drop in total blood volume due, essentially, to a marked decrease in red blood cell volume. With the other types of gelatin there was also a decrease in red blood cell volume, but it was compensated by an increase in plasma volume most striking, with 8 per cent and 6 per cent gelatin. The cells removed for samples cannot account for the decrease observed in the red blood cell volume, nor was such a marked decrease observed in those experiments in which whole blood was the infusing agent. Except for the 4 per cent gelatin the total blood volume after 24 hours was even lower, this further drop now being due to plasma loss. It appears that the presence of gelatin in the circulation has a tendency to displace red blood cells from the circulation.

3. Effect on sedimentation rate: The sedimentation rate was markedly increased with all types of gelatin. It was most evident with 8 per cent "medium" or "high plunge" pigskin and 6 per cent bone gelatin. Conglutination of the red blood cells was observed.

4. Other findings: Prothrombin determinations were carried out in a number of animals. Generally, the prothrombin content of the plasma was lowered. As expected, a definite hypoproteinemia was present 24 and 48 hours after the experiment. A large amount of the animals' plasma had been removed, and although these proteins were replaced immediately by gelatin proteins, the latter more or less rapidly left the circulation and were not replenished rapidly from the body. Although there was a wide difference in the protein decrease in different animals, the average deficiency 24 hours later amounted to 35 per cent. Hueper, Robscheit Robbins and collaborators and others (33, 35), have called attention to this and have presented evidence that gelatin may interfere with formation and restoration of blood proteins. These authors have stated that certain pathologic changes were observed, but Morehead and Little feel that "the lesions seen in the control animals did not differ fundamentally from those seen in the ones, which had received injections of gelatin" (30).

TABLE V.—BLOOD AND PLASMA VOLUME CHANGES

Gelatin code No. and concentration	Blood volume Per cent change from control		Plasma volume Per cent change from control	
	After 5th infusion	24 hrs. later	After 5th infusion	24 hrs. later
A & B (8%)	+ 1	− 8	+26	+ 6
C (4%)	−17	−14	− 6	0
E (7%)	− 7	−16	+ 9	− 5
F (7%)	−26	−28	− 2	+17
G (6%)	− 6	−17	+20	0

In earlier work, some random samples of gelatin caused shock reactions and at times were fatal. This did not occur with any of the specimens employed for this study. Delayed reactions may have occurred but would be masked by the shocking effect of the experimental procedure. It is our belief that there were no such delayed reactions because those animals with a high factor of probability of survival, and therefore a good prognosis for recovery, generally followed the expected course. There may possibly have been such a delayed reaction with the use of 6 per cent bone gelatin because animals with good factor of probability of survival and which were alive 24 hours after the experiment, subsequently expired.

DISCUSSION

After a careful review and thorough statistical analysis of our results, we arrived at the

conclusion that, if a proper volume and concentration of gelatin were used, it would prove effective in overcoming the effects of repeated bleedings. The response and survival of animals as a result of the gelatin infusions were clinically and statistically on a par to that of animals reinfused with their own blood. Our experience indicates that it is important that the volume reinfused should replace that which was removed, and that a concentration of 6 per cent gelatin or more produced the best results. Thus, 2 per cent gelatin was quite ineffective, even though the volume was adequate. It is probable that there are differences between the varieties of gelatins used in higher concentrations, but these differences could not be demonstrated statistically in our experiments. Despite the failure to show significant superiority of one or another gelatin, we were impressed by the response and survival of the experimental animals to gelatin E. Although gelatin G, which was least degraded, might be considered superior because it remained longer in the circulation, the ultimate effect on indefinite survival seems to be inferior to that of the other forms of high concentration gelatin.

Little and Wells (27) report that autoclaved gelatin does not pass through the walls of injured capillaries more readily than unautoclaved gelatin. If, as it appears from our results, there is no marked superiority of any particular gelatin preparation if a sufficient concentration and volume are used, the choice depends on other considerations. Method of preparation is one such consideration. We were not informed in all details of the technique of preparing the products furnished to us, but different methods are known to be employed by different manufacturers. That method which gives the most consistent end product is to be preferred. Ease of manufacture is another consideration. It is fundamentally important that the product should be nonpyrogenic and free from adverse reactions. As stated previously, in our earlier work, some random, poorly prepared material was itself shock-producing. None of the materials we tested had such an unfavorable effect, and only one was pyrogenic. This last preparation, nevertheless, proved quite effective in our experiments, confirming our earlier experience that the presence of small amounts of pyrogens did not necessarily or in every case interfere with the restorative properties of a preparation. Nevertheless, gelatin for intravenous use can and must be made free from pyrogens. All gelatins cause conglutination of the red blood cells and an increased sedimentation rate. This may or may not (21) interfere with blood grouping and cross-matching procedures in the event blood transfusion is employed. In none of our work did we experience any bad results that could be attributed to this effect of gelatin on the erythrocytes.

Although the gelatin with minimal hydrolysis (G) remained considerably longer in the circulation, even such gelatin escapes rather rapidly from the circulation and it does not have any more beneficial effect than the more hydrolyzed forms of gelatin. Since such gelatin is solid at ordinary room temperature, its administration becomes rather laborious. It must be warmed to liquefy and, if the infusion is not rapid, it may gel unless kept warm. This fact introduces a further problem of maintaining the gelatin liquid during administration. The delay introduced by the necessity for warming and the need of heating equipment during administration appear to be definite practical objections to the use of a solid gelatin preparation. From the viewpoint of speed and facility of administration, we would prefer a liquid gelatin preparation of 7 to 8 per cent concentration.

This study was primarily directed toward determining the relative efficacy of gelatins of different concentrations and different degrees of hydrolysis, but a discussion would be incomplete without a broader consideration of its value. Our experience and that of others establishes gelatin as an effective agent in overcoming plasma loss and shock resulting from such plasma loss. At the same time it must be recognized that gelatin does not replace the plasma proteins in the circulation, except for a limited period of time. Following the elimination of the gelatin, the plasma protein or blood loss or both, if extensive, results in a plasma protein depletion and anemia which may be restored slowly or rapidly, depending on many factors. The existence of a

low plasma protein content delays recovery, particularly if there is a complicating infection. In such cases, the plasma proteins should be restored as rapidly as possible to normal levels by plasma or whole blood administration and proper nutrition.

Gelatin is an effective agent in combatting shock due to plasma loss and should be a valuable addition in our therapy, if the gelatin is used with due regard to its properties and limitations.

SUMMARY

The efficacy of gelatin solutions in the treatment of hemorrhagic shock was tested.

Various brands of gelatin, gelatins with different degrees of hydrolysis and various concentrations of gelatin solutions were tried in our experiments.

Our method of repeated graded hemorrhages and reinfusion of the blood 30 minutes after each hemorrhage was used as control. In the assays of the gelatin solutions, the plasma of the withdrawn blood was replaced by a gelatin solution.

The factor of probability of survival and the critical carbon dioxide value were used to predict the chance of survival of the individual animal. Prolongation of the periods of survival served as criterion of the efficacy of the gelatin solutions.

Gelatin solutions of 2 per cent concentration do not prolong life of the shocked animal appreciably and therein resemble physiologic saline solution.

The best results were obtained with gelatin solutions of 6 and 8 per cent concentration. The effects of these solutions with the packed cells were as good statistically as reinfusion of whole blood.

The degree of hydrolysis of the gelatins, in the range tested by us, did not seem to be an important factor in the efficacy of the gelatin as plasma substitute.

Gelatin solutions must be pyrogen free and should be liquid at room temperature.

In the dog, gelatin is excreted rapidly in the urine, with the exception of 6 per cent bone gelatin, which left the circulation at a slower rate than the skin gelatins.

Gelatin solutions dilute the blood and lower hemoglobin and protein values. In some cases, plasma and red cells must be given later in the treatment.

Following our experience in the dog, we do not hesitate to recommend gelatin solution for use in patients. Gelatin cannot replace whole blood, nor is it a substitute for plasma, but has value as an inexpensive easily available agent to combat shock due to plasma loss. Our experience with the use of gelatin solution in the patient has been favorable.

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CIRCUMSCRIBED CHRONIC SUPPURATIVE MASTITIS SIMULATING CANCER

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A WOMAN, 44 years of age, sought our advice regarding a lump in her breast. This lump was first noticed 3 months previously and was not associated with pain. Physical examination revealed a hard nodular mass, adherent to the overlying skin, with typical *peau d'orange*, and retracted nipple, accompanied by enlarged, hard, nontender, homolateral axillary lymph nodes.

The patient was admitted to the hospital with a diagnosis of carcinoma of the breast and axillary metastases. Her leucocyte count was 7600 per cubic millimeter of blood with 60 per cent neutrophils. Her highest preoperative temperature and pulse were 98.6 degrees F. and 88 per minute respectively.

A radical mastectomy was done and revealed a hard, circumscribed, unencapsulated mass measuring 9.0 by 6.0 by 3.5 centimeters, and several enlarged, hard axillary lymph nodes. Before sending the amputated breast to the pathology department the tumor was sectioned and, with considerable chagrin for all concerned, it was found that the dense fibrous tissue constituting the tumor mass contained a central abscess, approximately 2.0 centimeters in diameter, filled with thick, yellowish green pus.

During the following years this type of lesion was observed at fairly regular intervals, once or twice a year, sometimes with minor variations in symptomatology, but with fairly consistent pathological findings, and in numerous instances presented great difficulty in differentiation from carcinoma of the breast.

Because of the close similarity between cancer and this benign condition and in order to determine if this condition should be considered as a distinct clinical entity, we reviewed all breast tumors removed at Gorgas Hospital from 1920 to 1945. This study included the relative incidence, etiology, duration, diagnosis, gross and microscopic pathology, and best methods of treatment of circumscribed chronic suppurative mastitis.

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THE DATA

Incidence. This lesion was not of common occurrence; from 1921 to 1939, a period of 18 years, only 17 cases were seen. During 1939 5 cases were encountered, in 1942 there were 3 cases, and never more than 1 or 2 in the remaining years. A total of 32 cases in 25 years were selected for study. Its relative incidence as compared with carcinoma was approximately 1 to 5.

Age. This disease was one of middle age. One patient was under 20 years, 2 between 20 and 29 years, 8 between 30 and 39, 14 between 40 and 49, 5 between 50 and 59, and 2 were over 60 years of age.

Race and previous pregnancies. There was no good evidence of any relationship between the incidence of this condition and race; 7 of the women were white and 25 negro, a ratio of 1 to 5, which accurately reflected the hospital proportion of these two races. The negro women had more pregnancies than the white women, the average number for whites being 2, ranging from 1 to 5; and for negro 5, ranging from none, in 1 instance, to 18.

Previous treatment. Three women had had incision and drainage of the involved breast, one 3 weeks, another 2 years, and a third 17 years previously. This last infection occurred 10 days postpartum and was the only one directly associated with a puerperal abscess. Three patients had had previous incision and drainage of the opposite breast, 1 abscess of which could be classed as puerperal in origin. One other patient had a radical mastectomy of the opposite breast done elsewhere on the Isthmus; no tissue was available for pathological study. These instances were the only

evidence of previous breast disease recorded in the case histories, although it seemed inconceivable that "caked breasts," should not have occurred in some cases. There was no history of trauma in the entire series.

Duration. The duration of this condition before the patients sought treatment was difficult to determine with accuracy. A few admitted having a lump in the breast for months but the great majority insisted that it had been present for only 2 weeks or less: in 14 for 3 to 7 days, in 7 for 8 to 16 days, in 6 for 3 to 4 weeks, in 4 for 3 months, and in 1 for 3 years. The older women were more or less reticent regarding their breast tumors; this was especially true of negro women who had a great fear of operations. However, the patients were questioned very carefully on this particular point and their answers were at variance with the operative findings. It is difficult to picture a mass the size of a tennis ball, with a dense fibrous wall an inch or more thick surrounding a central pus pocket containing a dram of pus, developing in 2 weeks or less.

Approximately one-third of the patients noticed that the tumor mass had enlarged rapidly in the last few days before admission to the hospital. We believe these lesions to be long standing and will elaborate this phase further under the pathological discussion.

Symptoms. The symptoms were varied: "lump" in breast in 30, swelling of breast in 3, pain at onset in 11, late pain in 5, no pain in 6, "heavy sensation" in 3, "squeezing sensation" in 1, "burning" in 1, discomfort in 1, tenderness in 6, pain in nipple in 1, itching of nipple in 1, discharge from nipple in 2, tumor enlarging rapidly in 9, fever (early) in 5, swelling in axilla in 1. Of these the most important were the lump in the breast, the various interpretations of pain or discomfort, the early fever, and the recent rapid enlargement of the mass.

Physical findings. The tumor was described as hard in 19, indurated in 3, lobulated in 1, rough in outline in 1, firm in 9, nonfluctuant in 1, circumscribed in 3, nodular in 1, irregular in 2, regular in 3, stony in 1, adherent to skin in 11, not adherent to skin in 7, not adherent to underlying tissues in 5, movable in 4. The overlying skin was "orange peel" in 4, red in 1, and increased temperature was noted in 2. Five patients had retraction of the nipple and in 1 instance ulceration was present. The breast was tender in 8 but in 10 tenderness was recorded as being absent. The axillary glands were palpable in 9, not palpable in 5, hard in 3, and adherent to the skin in 1.

We are all familiar with the cardinal signs of moderately advanced breast cancer, the hard lump fixed in the breast tissue, flattening or dimpling of the overlying skin when squeezed gently, adherence of the tumor to the skin and underlying tissues, retraction of the nipple, poor transillumination of the breast, the "orange peel" skin, and enlarged, hard axillary lymph nodes. Circumscribed chronic suppurative mastitis may present any, or *all*, of these characteristics.

In this series of cases, the leucocyte count and the polymorphonuclear percentage were within normal limits in all but a few cases, and in no instance was an increase in eosinophils noted. Temperature in the 100 degrees F. group was observed in 25 per cent of the cases and there was only 1 instance of 101 degrees F. or more.

Diagnosis. The differential diagnosis of breast lesions is of the greatest importance. To overlook a malignancy is a serious mistake. With circumscribed chronic suppurative mastitis the problem of diagnosis is reversed, but no less important. The performance of a radical mastectomy where less extensive surgical treatment will suffice is also a grave error. Patients with circumscribed chronic suppurative mastitis are often seen in that stage of the disease which most closely simulates cancer and hence differentiation of these two diseases is difficult and requires careful evaluation of all available information.

The duration of the symptoms is important in spite of the fact that the operative findings point to a lesion of long standing. The history of 2 weeks' or less duration with recent rapid enlargement of the tumor mass should be of maximum importance in the differentiation as this is unlike the progress of a malignant tumor.

Pain at the onset always points toward an inflammatory lesion although this may vary with the individual and in some instances be entirely absent. It should also be remembered

that pain may be present in malignant tumors that have attained this stage of development.

The symptom of early fever is less reliable, and by the time the patient enters the hospital will have subsided.

Tenderness on palpation is of about the same value as pain; it will vary with the individual and may be absent in half the cases. It, too, can be present in a malignant tumor that has reached these proportions.

Increased surface temperature or redness over the lesion is rare but, if present, points very strongly toward inflammation.

After careful evaluation of the symptoms and physical findings there will remain about one-third of the cases in which surgical exploration is necessary for diagnosis.

Preoperative biopsy for breast tumors, including aspirations, punch biopsies, and those procedures which remove only small bits of tissue we consider entirely inadequate. Positive findings in borderline cases may be inconclusive and negative reports simply show there is no evidence of malignancy in the tissue submitted. In this institution frozen sections are rarely done except under special circumstances. After several unfortunate experiences the procedure was discarded as unreliable for breast tumors and a rapid 24 or 48 hour paraffin method substituted. We have made it a rule to send all of the tumor to the pathologist for biopsy whenever possible, even should it include the entire breast. To do less is unfair to the patient and the pathologist.

The preoperative diagnoses in this series were: chronic mastitis, 5; chronic cystic mastitis, 1; abscess, 7; tumor, type undetermined, 8; carcinoma, 7; carcinoma with axillary metastases, 4.

PATHOLOGY

Although minor variations may be present, both the gross and microscopic pathologic features of this lesion are distinctive. The tumor varies considerably in size. When palpated through the skin such terms as "size of a large walnut," "hen's egg," "plum," "lime," and "orange" were employed. In actual measurement the tumors varied from the smallest, 2.0 centimeters in diameter, to the largest 11.0 by 9.0 by 5.0 centimeters. The shape is ovoid rather than round. The tumors cannot be peeled away from the surrounding breast parenchyma without great difficulty as no actual cleavage planes are present; sharp dissection is necessary either at the operating room table or at the pathological examining board.

The essential characteristics of the lesion are best seen if the tumor is hemisected. There will be found a central abscess filled with gray, yellowish gray, or greenish pus. This purulent center is always small in relation to the mass; often it measures only 0.5 centimeter in diameter even in the largest tumors. Occasionally the abscess measures 5.0 centimeters in its greatest dimension but this is distinctly unusual. An average abscess measures 1.0 to 1.5 centimeters in diameter. This pus is rather thick and does not flow easily. When the pus is removed a shaggy, gray, or grayish green lining is observed. In a few specimens two or three small abscesses of a similar nature are found instead of one central abscess. Occasionally the larger abscess communicates by narrow channels with smaller satellite abscesses.

The bulk of the tumor is composed of dense, firm, white tissue surrounding the abscess. This can be cut with moderate resistance and a slightly gritty sensation. Frequently the tissue is so hard as to be grossly indistinguishable carcinoma. The wall of the abscess measures from 1.0 to 5.0 centimeters in thickness. For this reason, if the tumor is cut tangentially or if the section misses the abscess, only firm white tissue strongly resembling carcinoma is found. The tumor blends gradually into the adjacent parenchyma which is rubbery and rolls under the cutting knife. One side of the tumor may be close enough to the skin to be adherent to it and it is in these cases that wrinkling of the skin is prominent.

The axillary lymph nodes are enlarged, some measuring as much as 3.0 centimeters in their greatest dimension. They are discrete and firm, and on sectioning appear uniformly gray or somewhat mottled but no hard white areas indicative of metastases are seen.

Microscopically the abscess is filled with polymorphonuclear leucocytes, generally in a fair state of preservation. Occasionally many fat-filled macrophages and a few lymphocytes

are mixed with the neutrophils. There is no distinct lining to the abscess but in a few cases fragments of ductule epithelium can be seen within it. The wall of the abscess consists of connective tissue or granulation tissue heavily infiltrated with lymphocytes and plasma cells. Occasionally large areas are found which are occupied by fat-filled mononuclear cells. Eosinophils are not common, but in a few cases areas can be found in which there is considerable eosinophilic infiltration. In most of the specimens giant cells are absent but in some of the older lesions many giant cells of the chronic irritation form can be identified. Most of these are present in the dense connective tissue constituting the wall of the abscess, although they may be found lining the abscess. These cytologic components vary considerably in number and conspicuousness. The outer layer of the abscess wall blends gradually into the surrounding breast tissue.

In smears of the purulent material stained by Gram's method can be found gram positive cocci resembling staphylococci. In the few instances in which cultures of the pus were taken Staphylococcus aureus or Staphylococcus albus was grown.

In the breast tissue surrounding this tumor there are generally found histologic changes of significance. The most important of these is a periductular inflammatory reaction with infiltration by lymphocytes and plasma cells. The lumina of the ductules generally are free of exudate. This inflammatory reaction is often marked and is found at some distance from the tumor. Occasionally there may be an inflammatory infiltrate between the acini, associated with the periductular inflammatory reaction. The largest ducts of the breast are almost always free of pus and there is little inflammation around them.

All of the sections were carefully reviewed; no evidence of malignancy was found in any of them. The lesion of so-called "chronic cystic mastitis," a noninflammatory disease, is not a feature of this syndrome and the histologic changes of that condition were not noted in these cases. Some adenomatous proliferation of the acinar epithelium can occasionally be seen but this condition does not appear to be significant.

The axillary lymph nodes show diffuse lymphoid hyperplasia and some fibrosis. The capsules are intact. There is little perilymphatic inflammatory reaction. In none was evidence of malignancy found. No abscesses were noted within the nodes.

TREATMENT

Surgical procedures for the relief of circumscribed chronic suppurative mastitis included incision, drainage, and biopsy; excision of the inflammatory mass; simple mastectomy; mastectomy with resection of the axilla; and radical mastectomy. The procedures in our series representing the cases of 9 well qualified surgeons during this period of 25 years were: incision, drainage, and biopsy, 3; excision of tumor, 10; mastectomy, simple, 8; mastectomy with resection of axilla, 3; frozen section biopsy and radical mastectomy, 1; radical mastectomy, 7.

We have found simple incision and drainage a poor operation for this disease; the lesion is likely to recur sooner or later and such treatment will invariably leave a hard lump to worry the patient and surgeon.

Excision of the tumor mass is an excellent operation for middle-aged women with large breasts and a considerable amount of normal breast tissue. The tumor will usually be well circumscribed; it should be excised well beyond the limits of the mass, and sectioned immediately. If a central pocket of pus is present the wound is drained in the dependent portion, the skin sutured, and the entire inflammatory mass sent to the pathologist. We believe that the possibility of the development of a malignant condition is no greater in this type of chronic abscess than in normal breasts. However, the possibility of a malignant tumor breaking down and forming a central necrotic area must always be kept in mind.

With women past the menopause and having small atrophic breasts and a large heavy tumor mass, we believe the best procedure to be a simple mastectomy with extension of the incision toward the axilla to allow for the removal of axillary lymph nodes if it is deemed advisable. This is still a simple operation, causing little shock and it can easily be under gas or intravenous anesthesia.

The radical mastectomy operations in our series represented errors in surgical diagnosis except in 1 instance of an incorrect frozen section biopsy report. These errors, resulting in a major operation being done for a benign condition, are due mainly to one factor, fear of cancer. We allowed the typical physical findings of carcinoma to obscure the value of the less distinctive clinical symptoms.

In our opinion the best surgical treatment for a patient with a tumor of the breast in which the differential diagnosis rests between cancer and circumscribed chronic suppurative mastitis is as follows: first decide whether the tumor mass alone or the entire breast is to be removed, then proceed with the excision or simple mastectomy, placing the incision so that its site may be included in a radical mastectomy should such become necessary for malignancy. After the tumor or breast has been removed have it immediately sectioned on a separate table, preferably by the pathologist. Careful examination of the tumor at this time will solve the problem in most instances. The tumor should not be incised *in situ*; pus, if present, will likely contaminate the entire wound and may prolong the convalescence. The wound is closed as following a clean operation, with drainage in the dependent portion to allow for serous oozing and low grade infection. Send all tissues removed to the pathologist for careful study by paraffin sections which can be prepared in 24 or 48 hours. By following this technique we believe that a certain number of patients may be spared the more serious and mutilating radical mastectomy.

DISCUSSION

Despite the definiteness of this clinical and pathologic entity, a review of the standard current textbooks of surgery, pathology, and monographs on the diseases of the breast reveals little or no consideration of this problem. Only Hertzler in his monograph *Surgical Pathology of the Mammary Gland* has described in detail an essentially similar condition, and his views are so sound and so lucidly expressed that they should be examined in the original.

Nevertheless, this is not a new disease, nor is its recognition recent. It was described in the last century.

Under the title of "Chronic Productive Mastitis" Ewing wrote:

> "(2) A somewhat different form of mastitis was first described by Werhner as cirrhosis mammae, by Velpeau as 'induration chronique en masse,' and by Virchow as 'elephantiasis dura.' It is much less frequent than the common cystic disease. Billroth was long uncertain of its existence, but described a very advanced case with extensive cicatricial contraction and deformity. Labbe and Coyne described a case in which there was diffuse growth of very cellular connective tissue infiltrated with round cells, while a small collection of pus was found in the axillary border of the gland.
>
> "Koenig recognized a rare form of diffuse chronic mastitis with a painful onset, and a marked tendency to atrophy. R. Williams collected several cases in both sexes. Many cases of apparently suppurative mastitis with cicatrization and even calcification (Bryk, Hendoupe) he classifies as circumscribed chronic mastitis. They should be separated from the non-suppurative diffuse inflammations."

By the very names which these older writers employed to distinguish this truly inflammatory state from the so-called "chronic cystic mastitis," an entirely different condition, we may recognize their familiarity with the process under consideration in this paper. However, as so often happens, the observations of older men are forgotten and require redescription and re-emphasis.

In the past decade, however, there has been described, under the title of plasma cell mastitis, an entity which may overlap to some extent the type of case presented in this paper. It is not our purpose critically to evaluate plasma cell mastitis but it may be noted that some dissatisfaction has been expressed both with the entity as described and with its name. Reference should be made to the descriptions of Adair, Cheatle and Cutler (2), Rodman and Ingleby, Cromar, Cutler (5), and Miller.

The microscopic features of plasma cell mastitis as noted by Adair included: (1) marked infiltration of the breast with plasma cells; (2) proliferation of the cells lining the milk duct, giving the appearance of comedo carcinoma; and (3) formation of giant cells suggesting tuberculous mastitis.

Although in their description of plasma cell mastitis Cheatle and Cutler stated "The affected portions of the breast are the seat of an active, acute and subacute exudative inflammation with a high proportion of polynuclear

leucocytes in the exudate as well as lymphocytes and plasma cells," Cole and Rossiter in writing of the same condition affirmed that "The lesion does not suppurate."

In our patients the essential feature of the lesion was the presence of a small purulent central abscess. In the surrounding tissue could be seen, in many instances, an intense plasma cell infiltrate, and occasionally giant cells distributed in a histologic pattern somewhat similar to that depicted in the articles on plasma cell mastitis. We have difficulty, however, in regarding this as unique, and agree with Payne that "plasma cells are nothing but the expression of a chronic inflammation of long duration. They are not pathognomonic of anything." Although there was periductal and periacinar plasma cell infiltration in some cases this was almost always limited to the wall of the abscess and in the immediately adjacent tissue, whereas the description of plasma cell mastitis suggests a more diffuse process. Proliferation of the cells lining the milk ducts and giant cell formation giving the appearance of tuberculous mastitis were not features of our cases.

Probably the most dramatic difference between these two conditions is a clinical one. In plasma cell mastitis "the affection begins suddenly with pain, tenderness, diffuse swelling, and often axillary adenopathy. Fever is usually present and sometimes a slight rigor may herald the beginning of the disease" (2).

The pathogenesis of circumscribed chronic suppurative mastitis is not entirely clear but the lesion is inflammatory in character and bacterial in origin. We can only speculate as to the duration of the lesion and the method of infection. The periductule inflammatory reaction found in the adjacent or surrounding breast tissue in so many cases suggests that the bacteria gain entrance by way of the duct system of the breast. Although the wall of the abscess is often extremely thick and obviously of months' and possibly years' duration, the fair state of the neutrophils within the center of the abscess suggest that the purulent lesion is relatively recent. These discrepancies can be fused by the supposition that the lesion is old, of months' or years' duration, but that the infection smolders in a dormant fashion for a long time. Some unknown factor may cause an acute exacerbation of the symptoms with rapid enlargement of the tumor bringing it within the clinical horizon. The possibility exists that infection occurs during the puerperium. Hematogenous spread with localization of bacteria in a previously damaged breast must also be considered.

In conclusion, we believe that circumscribed chronic suppurative mastitis is a distinct entity, clinically, surgically, and pathologically, and should be recognized more widely as such. Because of the number of radical mastectomies which have been performed for this benign condition, textbooks of surgery should provide a more complete description of this disease and its method of treatment. Clinically circumscribed chronic suppurative mastitis may simulate cancer so closely that differentiation is impossible without pathologic examination of the tumor. If the principles of treatment as outlined are followed, patients with this benign lesion may be spared radical treatment, whereas those with malignant tumors will in no way be deprived of the full diagnostic and surgical efforts required in the treatment of cancer.

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A COMPARISON OF SUTURE AND NONSUTURE METHODS FOR THE ANASTOMOSIS OF VEINS

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THE introduction of an improved method of blood vessel anastomosis by Blakemore and Lord (3) in 1942 put a new and practical tool into the hands of the vascular surgeon. This method made use of the principle that two vessel ends can be successfully joined over a tube of inert metal (vitallium), provided the inside of the tube be lined with intima; thus it reaffirmed the long known axiom (8) that intimal integrity and continuity are the essence of permanent blood vessel patency. The advantages of the new nonsuture method were asserted to be chiefly: (1) the technical ease and speed with which the anastomosis could be performed, especially under battle conditions where the immediate re-establishing of blood supply was essential to the life of a part, and (2) the fact that a gap could be bridged.

This nonsuture anastomosis was in fact first devised as a means of bridging arterial defects (3, 4); a segment of prepared vein was used to line the gap between the divided ends of an artery. However, the method has since been applied by Blakemore (2) and others to vascular problems in which there is no defect to be bridged; i.e. to cases amenable to the old direct suture method of anastomosis (5, 6). Notable among such cases has been the portal caval anastomosis for the relief of portal hypertension (2). Such a procedure may consist in (1) an end-to-end anastomosis between the proximal ends of the divided splenic and left renal veins following removal of the left kidney and spleen, or it may mean (2) the anastomosis of the divided distal end of the portal vein to the *side* of the inferior vena cava.

The question therefore arises whether the newer nonsuture method is preferable to anastomosis by suture. In cases in which either procedure is feasible, is the nonsuture anastomosis better than the old direct suture method? And what are the advantages and disadvantages of each procedure? The results of the few reported cases in which the vitallium tube has been used are promising. The advantages of technical ease claimed for this procedure are undisputed. But current developments and the recently observed potentialities of blood vessel surgery demand a more thorough comparison of the two methods and their merits.

The primary consideration in all blood vessel surgery—far from being any refinement of technique *per se*—is, of course, the functional efficiency of the vessel as a conductor of blood. Compared to this all other factors are secondary and contributory in their importance. Unless a given procedure produces results at least comparable to those of other methods, no technical advantage justifies its use. A valid analysis and comparison of two such different methods would have to be on a functional basis. Anastomoses would have to be performed by each method under similar conditions and on the same vessels in a number of experimental animals, and delayed observations made of the functional patency of all these anastomoses. The purpose of this report is to present a summary of such observations.

PROCEDURE AND TECHNIQUE

The renal splenic vein anastomosis was considered singularly suited to this comparative study, since it would eliminate certain external and mechanical factors which might introduce an inconstant error. From a physiological standpoint, the pressure gradient between the portal and caval systems in normal dogs is small, 30 to 50 millimeters of water (1). This means that the sheer mechanical pressure effect of flowing blood in keeping the anastomosis open is reduced to a desirable minimum.

In these experiments dogs weighing between 15 and 25 kilograms were used. They were

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TABLE I.—RESULTS END-TO-SIDE SUTURE ANASTOMOSIS

Dog No.	Days after operation	Function	Microscopic
1	12 (Died)	Patent	No section.
2	16 (Died)	Thrombosed	No section.
3	75 (Sacrificed)	Patent	No thrombus.
4	74 (Sacrificed)	Patent	Slight intimal thickening.
24	25 (Sacrificed)	Patent	5 mm. thrombus along splenic vein.
25	25 (Sacrificed)	Patent	Slight intimal thickening.
26	27 (Sacrificed)	Patent	No thrombus.
28	32 (Sacrificed)	Patent	No thrombus.
32	28 (Sacrificed)	Patent	No thrombus.
50	70 (Sacrificed)	Patent	No thrombus.

anesthetized with intratracheal ether. In order to avoid errors of technical variation, the types of anastomoses were performed alternately and by the same operating team. At intervals of 12 to 75 days following operation autopsies were made on the dogs. The anastomoses were examined grossly for functional patency and thrombosis, and microscopically for intimal changes and the presence and type of thrombi.

Three series of operations were performed. No anticoagulant was used in any of these experiments.

In the first series the proximal end of the divided splenic vein was anastomosed into the side of the intact left renal vein. The anastomosis was done by the classic method of Carrel and Guthrie (5, 6). There were 10 dogs in this series.

In the second series, in which 11 dogs were used, the spleen and left kidney were removed and a suture anastomosis was performed between the proximal ends of the splenic and left renal veins. With fine silk and straight needles, three stay sutures were placed to insure proper alignment and a continuous running suture was employed with care to approximate intimal surfaces by everting the edges of the veins.

In the third series, after splenectomy and left nephrectomy, the ends of the renal and splenic veins were anastomosed over a vitallium tube by the method described in detail by Blakemore (2, 3, 4). The end of the splenic vein was brought through the tube and everted over its edge, being secured here by silk ligatures placed behind tying ridges on the outside of the tube. The end of the renal vein was then very carefully brought over the outside of the vein-lined tube and secured tightly by two silk ligatures, one behind the tying ridge and one just behind the edge of the tube. Twelve anastomoses were done in this series.

RESULTS

There were no operative or early postoperative deaths among the 33 dogs in the three groups of experiments.

In the first series (Table I), of the 10 end-to-side suture anastomoses, one was completely thrombosed after 16 days. Nine were functionally patent after periods of 12 to 74 days; of these, 1 showed a microscopic thrombus extending 5 millimeters along the lumen of the splenic vein, 2 showed negligible intimal thickening at the suture site and 5 were absolutely clear microscopically. No sections were made of the remaining 2. The silk suture material was unabsorbed even after 75 days, but the foreign body reaction was not remarkable. The over-all patency was 90 per cent.

Of the 11 end-to-end suture anastomoses, (Table II), 3 were completely obstructed by organized thrombi at 46, 55, and 51 days. Eight were functionally open after 13 to 55 days; 4 of these showed microscopic thrombosis which was functionally negligible; there was slight intimal thickening in 1; in the remaining 3 the anastomoses were clear. There was 72.7 per cent patency.

Of the 12 anastomoses performed by the nonsuture technique, only 2 were patent (Table III). Both of these were in animals sacrificed 14 days after operation. The remaining 10 were completely thrombosed after periods varying from 14 to 52 days. In all cases the thrombi were found to obliterate the vessel lumina throughout the entire length of the vitallium cannulas. There was microscopic evidence that the thrombotic process began in the renal end of the cannula and progressed down the splenic vein, since in most cases the fresher part of the thrombus was at the splenic end of the anastomosis. There was some recanalization, but this was of no functional

TABLE II.—RESULTS END-TO-END SUTURE ANASTOMOSIS

Dog No.	Days after operation	Function	Microscopic
6	27 (Sacrificed)	Patent	No thrombus. Silk suture has eroded intima at one point.
8	35 (Sacrificed)	Patent	Small organized thrombotic tag at suture line.
12	33 (Sacrificed)	Patent	Small organized thrombus in splenic vein.
14	27 (Sacrificed)	Patent	Small organized thrombus at suture line.
16	13 (Died)	Patent	No thrombus.
17	33 (Sacrificed)	Patent	One mm. thrombotic tag at suture site.
20	26 (Sacrificed)	Patent	No thrombus.
21	26 (Sacrificed)	Patent	Slight intimal thickening.
29	55 (Sacrificed)	Thrombosed	Organized thrombus filling entire lumen.
33	51 (Sacrificed)	Thrombosed	No section
34	46 (Sacrificed)	Thrombosed	Organized thrombus filling entire lumen.

TABLE III.—RESULTS NONSUTURE VITALLIUM CANNULA ANASTOMOSIS

Dog No.	Days after operation	Function	Microscopic
5	27 (Sacrificed)	Thrombosed	Organized thrombus completely filling lumen.
7	14 (Sacrificed)	Thrombosed	Fresh thrombus filling lumen inside tube.
15	28 (Sacrificed)	Thrombosed	Old thrombus filling entire tube
17	33 (Sacrificed)	Thrombosed	Old thrombus filling entire lumen
18	14 (Sacrificed)	Patent	No thrombus
19	34 (Sacrificed)	Thrombosed	Old thrombus filling entire lumen.
22	27 (Sacrificed)	Thrombosed	Old thrombus filling entire lumen.
23	26 (Sacrificed)	Thrombosed	Old thrombus filling entire lumen.
27	27 (Sacrificed)	Thrombosed	Old thrombus filling entire lumen.
30	14 (Sacrificed)	Patent	Fresh thrombus present in each end of tube.
31	52 (Sacrificed)	Thrombosed	No section.
9	33 (Sacrificed)	Thrombosed	Old thrombus filling entire lumen.

importance. In this group there was 17.2 per cent patency.

COMMENT

The results of these experiments indicate that in vein anastomosis, through which the blood flow is relatively small, e.g. splenic renal shunt, the suture method judged by functional patency is superior to the nonsuture method.

The fact that the nonsuture technique has met with greater success in arterial anastomosis than in this series may be attributed partly to the mechanical effect of the pressure of the arterial blood flow in maintaining patency. This factor should also contribute to comparably better results in direct suture arterial anastomoses.

In this connection, work by Murray and Janes, at Toronto, has shown that arterial anastomosis over metal bands leads to necrosis of the vessel wall with resulting hemorrhage in many cases. Suture anastomoses did not show this in any of their cases.

In addition to its demonstrated functional inferiority in this particular vein anastomosis, the nonsuture method has two important drawbacks pertinent to arterial as well as venal surgery. (1) It leaves a large foreign body in the tissues. (2) The metal tube is not expansile and hence the anastomosis cannot increase in size subsequently.

Regardless of the technique of anastomosis used in this portal caval shunt, the end-to-side would seem preferable to the end-to-end anastomosis because (1) it preserves the left kidney; and (2) it provides a greater flow of blood—from the left kidney—past the anastomosis, a factor which should be helpful in preventing thrombosis.

There is no implication here that the direct suture rivals the nonsuture method for bridging defects of arteries and veins. It is also apparent that the suturing of vessel ends is inferior to the vitallium tube when there is any appreciable tension on the anastomosis. In these important respects, the method of Blakemore is a major contribution. We conclude, however, that for cases in which a suture anastomosis can be performed without undue tension, this procedure is preferable to the nonsuture method, and remains the technique of choice.

SUMMARY

1. Experiments were performed on dogs to determine the relative merits of two accepted methods of blood vessel anastomosis: the di-

rect suture method of Carrel and Guthrie and the nonsuture method of Blakemore.

2. Anastomoses were performed (a) by suture between the proximal end of the divided splenic vein and the side of the renal vein, (b) by suture between the proximal end of the splenic vein and the proximal end of the renal vein, and (c) by the nonsuture vitallium tube method, between the proximal end of the splenic vein and the proximal end of the renal vein.

3. Delayed observations showed a higher percentage of functioning patent anastomoses in the suture groups (90% and 72.7%) than in the nonsuture group (17.2%).

4. It is concluded that in blood vessel anastomoses where there is no tension on the suture line and no defect to be bridged, the suture method of anastomosis is superior to the nonsuture method. In other cases the nonsuture technique of Blakemore is probably better.

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ORIGIN AND DEVELOPMENT OF THE ERECT POSTURE

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MAN with childlike innocence has always considered his erect posture a God given blessing. Milton in *Paradise Lost* said that in the Garden of Eden there were

> "..... all kind
> Of living creatures new to sight and strange."

But:

> "Two of far nobler shape, erect and tall,
> Godlike erect, with native honor clad
> In naked majesty seemed lords of all,
> And worthy seemed;"

Man's erect spine has been one of his greatest assets, yet to all intents and purposes also one of his greatest liabilities. Because of it the forelimbs have been divorced of their former function of locomotion and developed into organs of prehension. This fact has enabled man to become master of his domain. Despite this apparent superiority man's low back is a weak spot, a so called "Achilles' heel." Since man is the only living creature endowed with unconditional erect posture it may be well to examine this inheritance to shed new light on the problem created by his ability to walk erect.

The pelvis and hind limbs appeared first as keels or ridges supported by basal rods operated by extensions of the segmental muscles of the body wall. Later they became paddle-like and finally were bent downward and strengthened to support the body on land, and to cooperate with the pectoral limbs in pushing the body forward (2).

The pelvis arose in close association with other bodily functions, those of digestion and excretion, and also of reproduction in the discharge of eggs or living young in the female and of sperm in the male (Fig. 1). The pelvis thus arose around the cloaca and served as a base or platform for certain groups of muscles, those running forward along the lower surface of the abdomen, those running backward along the under and outer sides of the tail and a cone-shaped mass of muscles based on the pelvis and converging outward and downward to form the thigh muscles.

The ilium at first grew upward between the muscles of the back in front and the tail muscles behind. In so doing it passed to the outer sides of the ribs, being at first entirely free, but later becoming tied to them by connective tissue and ligaments and still later by bony connection.

Although we are not sure of the date when human posture evolved, we are quite certain that it became adjusted through a series of changes from arboreal to terrestrial existence (3). These changes can be readily observed by a comparative study, not only of living primates but of fossil material, beginning with the Devonian lobe-fin, Eusthenopteron foordi (Fig. 2 a), a prehistoric fish. In this animal, which existed about 350 million years ago, was formed the earliest evidence of a pelvic girdle consisting of a pair of bony rods on either side of the cloaca. It supported the pelvic fins which were moved by simple opposing groups made up of folds of the outer myomere.

Further development occurred after the lobe-fin fish came out on land. The iliac blades grew upward becoming attached to the sacral ribs and thus to the vertebral column. This is found in the earliest amphibians about 300 million years ago in the carboniferous age of which Eogyrinus (Fig. 2 b) is an example.

In the ancient amphibians such as Eryops megacephalus (Fig. 2 c) the pelvis was V-shaped. The body was slung by muscular straps attached to the pelvis much as the cables of a suspension bridge. The iliac blades were attached to the spine by ligamentous attachment to the sacral ribs. The limbs were widely spread apart and walking was cumbersome. The Cynognathus (Fig. 3 d) from the upper Triassic of South Africa, about 175 million years ago, represented an in-between stage of the reptile and the mammal. The limbs were adapted for running and there were many features of the skull, backbone, and limbs that approached those of mammals. The iliac blade

Fig. 1. The basic invention of the pelvis or bony foundation for the hind limbs. Underside of pelvic region of primitive shark, showing pelvic fins on either side of cloaca, which are keel-like folds supported by skeletal rods. (Reproduced from *Scientific American*, Oct. 1930, after W. K. Gregory.) *C*, cloaca, *B*, basal rods.

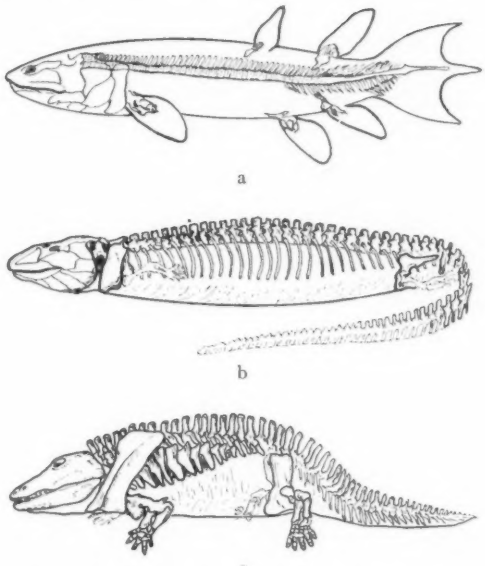

Fig. 2. Man's quadrupedal ancestors, comparison of: a, Devonian lobe-fin (Eusthenopteron foordi). b, Carboniferous amphibian (Eogyrinus). c, Permian amphibian (Eryops megacephalus). (Reproduced from *Proceedings of the American Philosophical Society* Vol. 67, 1928, after W. K. Gregory.)

was wider and was more firmly attached on a broader base to the spine.

As a representative of the next stage in development, the opposum (Fig. 3 e) may be studied (5). It retains, in the main, the leading characteristics of the skeleton of the older fossil animals. The iliac blade is elongated and inclined forward. The limbs contain five-toed grasping hands and feet, by which it made its way about in the trees. In these early mammals when the knees were drawn forward, the ilium also grew forward, almost parallel with the backbone to which it was now attached by means of the sacral vertebrae and their ligaments, the sacral ribs having become short and wide and fusing with the transverse processes of the sacral vertebrae.

The order of primates to which man belongs made its appearance early in Eocene times, about 60 million years ago in the form of an arboreal monkey-like animal, Notharctus (Fig. 4). Adaptation to tree climbing was quite well advanced which is obvious from certain features of the skeleton such as the grasping type of construction of the hind feet. It is highly significant that all of the known foot and limb bones of fossil lemurs, monkeys, and apes are unquestionably of arboreal type. Hence one must infer that the origin of the order of primates as a whole was arboreal. This fact is of importance in the question of man's origin and brings us to a consideration of the relationship between man and ape.

It is not certain when the separation of man from the primitive anthropoid stock occurred; however, it must have been during the Miocene epoch somewhat over 20 million years ago. No fossil showing the transformation has been found, and only by deductive and inductive inference have we been able to reach any conclusion. There is, however, some difference of opinion regarding man's origin. Professor Osborn states, "I personally had abandoned the anthropoid ape theory and I advanced the

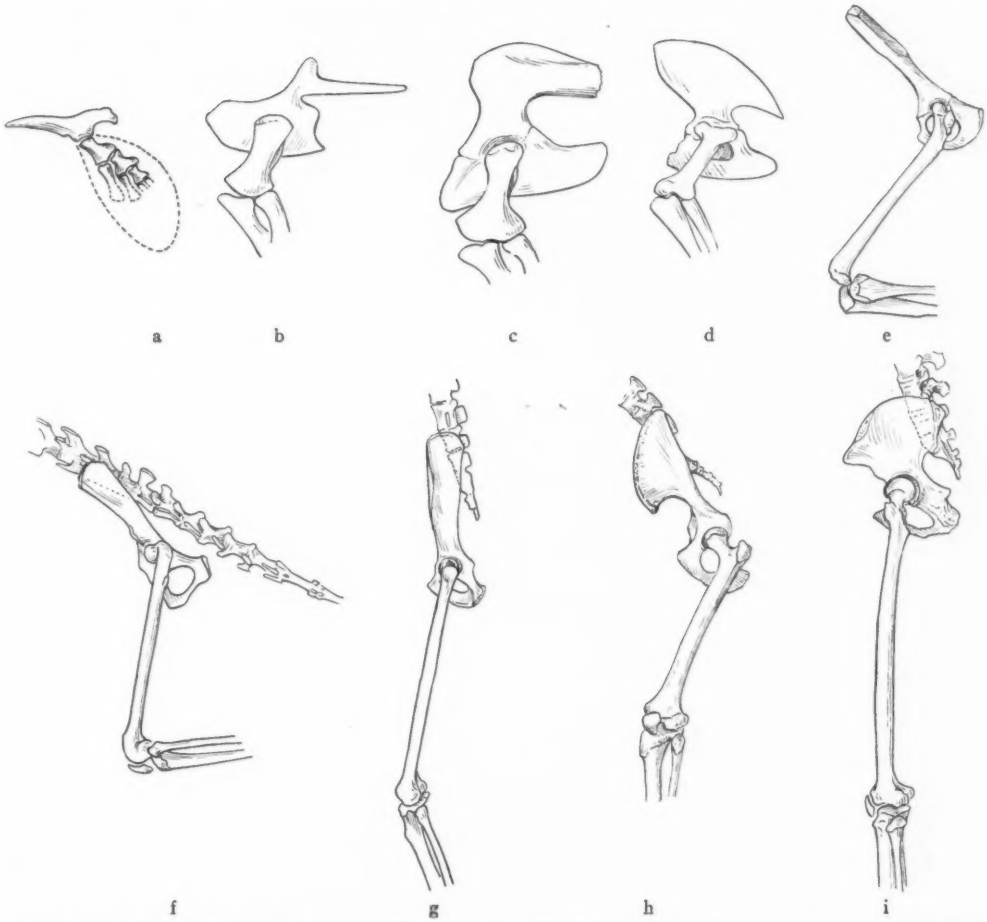

Fig. 3. Series progressive outward growth of ilium from fish to man. a, Lobe-finned ganoid (Eusthenopteron) of the Devonian period. b, Diplovertebron, early tetrapod. c, Primitive reptile (Limnoscelis). d, Advanced mammal-like reptile (Cynognathus). e, Primitive mammal (opposum). f, Primitive primate (lemur). g, Gibbon. h, Gorilla. i, Man. (Reproduced by Courtesy American Museum of Natural History, after W. K. Gregory.)

opinion that man has a long line of dawn ancestors and that the other theory rests upon a large amount of evidence which proves the kinship of anthropoid apes to man, but does not prove the ancestry of man through an anthropoid ape type." He further quotes Sir Arthur Keith, who is of the opposite opinion, stating that "all the evidence now at our disposal supports the conclusion that man has arisen from an anthropoid ape not higher in the zoologic scale than a chimpanzee" (7).

Man and ape possess certain characteristics in common, such as a high mentality, a prehensile hand, an erect or semierect posture, etc. However, there are certain skeletal and developmental differences which I propose to examine to obtain a clearer understanding of the evolution of the erect posture.

The gibbon, an East Asiatic tree-living descendant of the first family of tailless or manlike apes, is the only ape normally walking only on its hind legs when on the ground. The skel-

eton begins to be almost human (Fig. 3 g); however, the arms are excessively long because of its brachiating habits. Its pelvis begins to show incipient widening of the iliac blade as compared with the lemur (Fig. 3 f), one of a group of monkeys (Lemuroidea) which exist entirely in trees. In the lemur the ilium is narrow and is adapted for running and leaping. At first in the mammals the upper part of the ilium was triangular in cross section, its three surfaces being occupied respectively by the muscles of the upper side of the backbone, by the iliacus muscles in front and by the gluteal muscles on the outer side. When the primates began to sit upright, resting themselves on their folded legs and on the lower ends of the pelvis the iliac muscles served to check them from falling forward. Thus with increased size of these two muscles the blade of the ilium began to grow outward in a transverse plane, the chief successive steps in this broadening process being recorded in the lemurs, monkeys, apes, and man (Fig. 3 f, g, h, and i).

Since the gibbon has been endowed by nature with the ability to walk upright it may be well to pause at this point and learn how this came about. The body of the primitive quadruped is slung between two suspension towers, which are the pelvic and pectoral girdles. The gibbon has succeeded in turning this suspension bridge up at right angles to its original horizontal position and in balancing it on the rear tower represented by the pelvic girdle. Thus nature has worked out in this animal the basic invention for upright or bipedal progression. This step can be seen in the viscera which approach the human type in a number of ways, and in the details of construction of its pelvis.

The gibbon learned to run on its hind legs by first learning the habit of sitting upright, and secondly by the habit of brachiating or climbing with the arms raised above the head and the body suspended beneath the branches. The habit of sitting upright conditioned the first steps in the remodeling of the pelvis, especially the flattening of the ilium in the transverse plane. The habit of brachiating conditioned the extension to and upon the ilium of certain muscles of the loins and abdomen, thereby being better able to support the viscera, pelvis, and hind limbs when the body was suspended by the arms. In addition to climbing the gibbon makes enormous leaps from one branch to another, and in so doing has developed great extension backward of the thigh muscles so that they may be nearly parallel with the backbone. Thus he is able to walk when on the ground.

Further widening of the iliac crest together with an expansion of the iliac and gluteal muscles is seen in the gorilla (Fig. 5 c). This is further conditioned by the habit of sitting and walking upright on the ground. The gorilla, because of its great weight must of necessity be principally terrestrial, however it may take to the trees under certain conditions.

There is such a striking resemblance between the anthropoids and ourselves in external form and in their attitudes, also in their internal structure, particularly when studied in captivity, that we are apt to overlook the radical distinction in their mode of locomotion. In man, his whole weight is poised on a very narrow pedestal in direct opposition to the erect posture. If he declined at all from it he would be forced to the earth, but for the predominance in the back and the legs of the extensors over the flexors. The position of the ape in nature is just the reverse. He hangs and moves about among the trees by means of his long and powerful arms. He is thus sustained not from below, but from above; whereby his weight would soon bring him to earth, except for the immense power of his flexor arm muscles.

Various investigators have reported their studies of dissected material, and seem to be in general agreement that the muscle pattern of apes and man is similar; the main difference being in function and thus also in comparative size. For instance the gluteal muscles in quadrumanes are small and weak. Thus we assume that it is for this reason that the apes are unable to stand erect or stand on one leg as we do; whereas the real distinction is in the position of these muscles thus accomplishing a different function, mainly that of leaping. Man, however, does not leap well, and consequently by a priori reasoning we might assume that his glutei are small. This we know is not true. Again certain animals such as the horse cannot

stand erect. The secret of the functional difference is the position of the focal point of action. In man the external surface of the short broad ilium looks outward like the acetabulum. The fibers of the gluteus medius converge from a broad origin to the great trochanter; the whole arrangement acts to prevent the body from sinking to one side when supported by the opposite leg. It also assists the gluteus maximus and the psoas in preserving the balance forward and backward required in ordinary progression (8).

In apes the external surface of the ilium looks upward or backward while the acetabulum still looks outward as in man. Thus the acetabulum is at right angles with the ilium, which is long and narrow so that the fibers of the gluteus run nearly parallel to each other and the muscle is inserted at the end and not, as in man, down the outer side of the trochanter. Thus the leverage arm acts to greater advantage in man, aiding pelvic balance in walking and in the erect posture. The glutei, semitendinosus and biceps support the trunk behind and the gracilis and sartorius antagonize them in front. In man the glutei and long flexors of the leg have two sets of function according to whether or not they take their fixed point of function from above or below. This means that they may be used either for moving the legs by themselves or for acting powerfully upon the trunk as in locomotion. The human pelvis is likewise fitted in many other ways to act as a bony anchor for the muscles that tie in the abdominal viscera, and as a base for the powerful thigh and back muscles that hold the body erect.

Sir Arthur Keith has divided the evolution of the erect posture into three phases, the first, the hylobatian or gibbon type, represented by fossil remains found in Pliocene and Miocene deposits of Europe, parts of which very closely resemble the modern gibbon. He therefore assumes that they have come through unchanged. The next phase is that of the great anthropoid or troglodyte stage of which the chimpanzee is the most generalized surviving member whose upper and lower limbs are developed to a more or less equal degree. The gorilla also in this group, however, shows specialized development of the lower limbs. The third or plantigrade stage is represented by changes confined principally to the lower limbs. The knees and thigh extended and lengthened, the pelvis was modified and the muscles and bones assumed human form. We cannot fix the exact geological date and no fossil showing the transformation has been found. It is assumed that the geological date is in Miocene or Oligocene times, about 20 to 35 million years ago (6).

Fig. 4. Reconstructed skeleton of Notharctus, founder of the primates: A North American of Eocene times. (Reproduced by Courtesy of American Museum of Natural History, after W. K. Gregory.)

Fossil man has contributed little to our knowledge of when human posture evolved. We know that his posture was crouching in character, similar to the apes. Marcellin Boule in describing the so-called Neanderthal skeleton from La Chapelle - Aux Saints states that "the vertebral column was short and massive. The first vertebrae are much more like those of a chimpanzee than those of a man. Their spinous processes are long, lying at right angles to the axis of the vertebral column, instead of inclining backward and they are not bifurcated at the end.

"These peculiarities seem to indicate in the cervical region of the vertebral column either

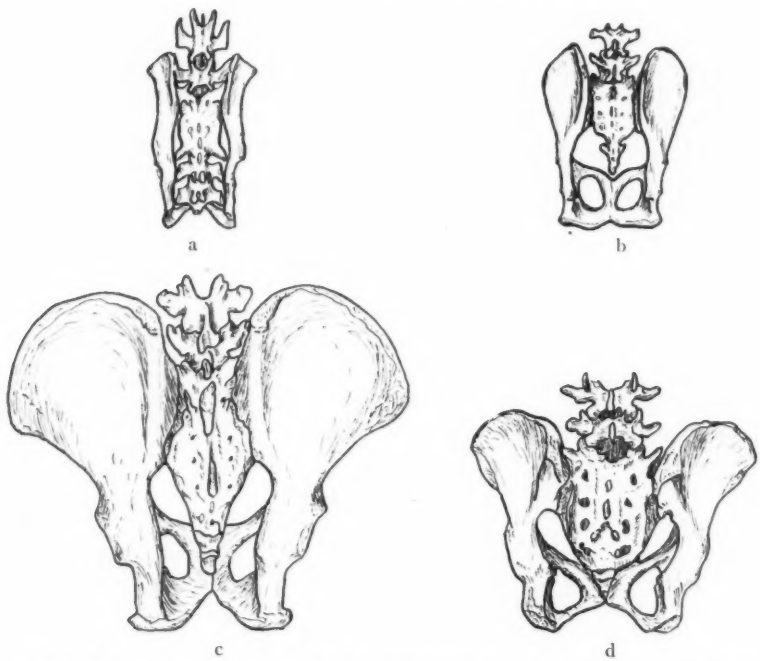

Fig. 5. Progressive widening of the pelvis and sacrum in Primates. a, Lemur, with long narrow ilia adapted for leaping. b, Gibbon, incipient widening of iliac blade. c, Gorilla. d, Man. (Reproduced by Courtesy American Museum of Natural History, after W. K. Gregory.)

a complete absence of curves or a slight curve in a direction opposite to that in modern man, prolonging the dorsal curve as occurs in anthropoid apes, such as chimpanzee.

"The vertebrae of the other regions are not so well preserved. It would seem as if the lumbar curve were less pronounced than in the majority of modern men. The portions of the sacrum which we possess point to narrow sacral vertebrae slightly arched and deeply set between the iliac bone. These are Simian characteristics" (1).

Thus Marcellin Boule gives account of the somewhat crouching posture of one of the most recent of prehistoric men. It may be concluded therefore that if Neanderthal man still possessed a moderate crouching posture and retained Simian characteristics of his skeleton up to 25,000 years ago, that human posture as we know it today has finally evolved in that short span of time, however it is possible that fully erect forerunners of Homo sapiens (e.g. Piltdown man) may date back to upper Pliocene times around one million years ago (4). We may conclude further that the low back area together with the sacrum and pelvis remain in a state of flux because it is this portion of the skeleton which has undergone the greatest change in the synthesis of erect posture. The human skeleton as we know it today may be the best adaptation for the purpose to which it is being put, however it is axiomatic that nature develops by trial and error and that future millenia will produce a structure better adapted to the stresses and strain which the erect posture entails.

CONCLUSION

Human posture is shown to have evolved through a series of progressive changes, beginning with the prehistoric Devonian fish, 350 million years ago. Changes occurred which allowed the ancient amphibians some 50 million years later to become land dwellers. Because

of poor adaptation to terrestrial locomotion their efforts were probably limited simply to obtaining food with little attempt made to move for any distance.

Walking continued to be cumbersome in the ancient reptiles, whose limbs were widely spread apart and not yet well adapted for land use. However, progress was made by evolutionary changes and there evolved a creature between the reptile and mammal, which was actually able to run on land. From this Cynognathus which existed 175 million years ago has evolved the more highly developed Notharctus an arboreal monkey-like mammal.

The Notharctus was one of a great group of primitive primates and as such may be considered a representative progenitor of the order of primates to which man belongs. The ability to climb trees was possessed by this animal and later by other lemurs, monkeys, and apes. The only ape able to walk upright on the ground is the gibbon, an East Asiatic tree living descendant of the first family of man-like apes. The skeleton of this ape begins to appear almost human in type. Nature first endowed this ape with the ability to walk by up-ending one tower of the suspension bridge to which the shoulder and pelvic girdle, together with the spine, may be compared and balance it on its rear tower, represented by the pelvic girdle. The ability to walk upright was evolved from the habit of sitting upright and by the habit of brachiating or swinging from limb to limb.

The ability to walk has been perfected in the human through modification of the entire skeleton, but principally the pelvis and lumbosacral spine. It is true that certain apes can walk upright, however this gait may not be natural for them because the pelvis is not mechanically suited for such progression. The muscle pattern of ape and man is similar, yet there is a difference in function and in comparative size; and a difference in the focal point of action of the gluteal muscles which is the secret of human ability to walk. In the ape the external iliac surface points backward at right angles to the acetabulum, rather than externally or outward as in the human.

Thus human posture was evolved by progression from water onto land, then into the trees and to the ground again, and as this progress was made the skeleton was conditioned to the habits of the animal or the uses to which it would be put. Since man is the culmination of nature's efforts over many millions of years it may be inferred that the erect or orthograde posture is the ideal means of terrestrial progression, and that no further change will occur. However in the words of Professor William K. Gregory "evolution bears no evidence of a beginning and no prospect of an end", thus we may hope that a more perfect creature is yet to evolve.

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MALIGNANT LYMPHOMA

The Value of Radical Surgery in Selected Cases

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SURGERY as a therapeutic measure in malignant lymphoma has been generally abandoned and has been replaced by radiation therapy because the disease is regarded as essentially systemic. Recently, however, Gall expressed the belief that radical surgery has a definite place in the treatment of malignant lymphoma. In his series of 48 patients with the disease sufficiently localized to permit radical surgical excision, 19 survived two to three times longer than identical cases treated by radiation. From the Memorial Hospital, New York, Sugarbaker and Craver reported a 5 year survival rate in 24 per cent of patients with malignant lymphoma subjected to early surgical treatment.

During the past twenty years, I have not infrequently noticed that sufferers from malignant lymphoma lived 5 years and longer after surgical removal of a single tumor and belied the gloomy outlook which I had predicted from the microscopic section. This discrepancy between occasional long survival periods after operation and the discouraging viewpoint of most surgeons regarding malignant lymphoma, prompted me to review all primary lymphoid malignant tumors which have passed through the Pathological Department of St. Francis Hospital. From January, 1925, to December 1945, 234 cases of malignant lymphoma were examined in our laboratory. While histologic slides were available for personal study from all these cases, only 130 cases were used for this analysis because they had complete clinical records and had been followed up for a sufficient length of time to be of value. The material included in this survey comprises 30 autopsies and 116 surgical specimens from a total of 130 patients.

Aided by a Grant from the Field Army of the American Cancer Society. From the Department of Pathology, St. Francis Hospital and Sedgwick County Tumor Clinic.

Records were complete to the day of death for 98 patients, and 32 patients are still alive for periods of 5 years or longer after the histologic diagnosis of malignant lymphoma had been established.

CLASSIFICATION OF MALIGNANT LYMPHOMA

In cases of lymphoid tumors, the difficulty in distinguishing between an inflammatory and a neoplastic tumor, and the uncertainty of correlating histologic structure and clinical course is familiar to every pathologist. Many surgeons and pathologists call all lymphoid malignant growths simply lymphosarcoma and they point out the possible transformation of one process to another. They believe that these processes are not only genetically related but that fundamentally they are merely phases of the same disease. Ewing, on the other hand, insists on a rigid application of simple histologic principles in the classification of lymphoid tumors, even at the risk of carrying the anatomical distinctions too far.

During recent years, three attempts have been made to classify lymphoid tumors. Foot accepted the principles of the Lymphatic Tumor Registry and distinguished between reactions and tumors of lymphocytic and of reticulum cell origin, those with and without leucemia. Murray and Broders described four grades of lymphosarcoma based on the degree of cell differentiation. They employed similar criteria as used in grading of epithelial malignant growths, and believed that the histologic grade in primary lymphosarcoma bears a definite relation to the time of survival following operation.

In 1942 Gall and Mallory proposed a classification not regarding anatomical distribution of the lesions and blood manifestations. From their analysis of 545 cases they conclude that nothing in the histologic character of an individual lesion will permit a reliable forecast

Fig. 1. Inoperable neck tumor in 56 year old male. Biopsy by incision into a tumor which is firmly fixed to surrounding structures is not advisable. Aspiration biopsy revealed typical lymphoblastoma. Initial response to roentgen treatment good. In our material, one out of three noninflammatory neck tumors was a malignant lymphoma.

Fig. 2. Localized reticulocytoma of mandible in 5 year old girl. Total removal of lower jaw, without radiation, resulted in cure. No evidence of disease today, 10 years after operation.

as to the distribution of the process in other parts of the body, nor can it be determined whether leucemia is present or not, by histologic examination of a lesion.

The same authors found a great constancy of the reacting cell types in biopsies of the same case taken at different times; in only 23 per cent did the lesion become less differentiated in appearance. As to the possibility of histologic distinction of the different types in routine biopsy material they could apply their method easily in 94 per cent. Gall and Mallory's classification which is fundamentally cytologic has the advantage of conforming with the accepted usages of oncology, and it has more than academic value in the field of malignant lymphoma, since a reasonable degree of correlation could be demonstrated with the clinical course of the disease.

The cell types making up the various subgroups of malignant lymphoma correspond to the different stages of cell development as found in normal lymph nodes. A knowledge of the normal cytology of lymphoid tissue is therefore necessary. According to Maximow, the supporting stroma in lymphoid tissue consists of a framework of argyrophilic fibers intimately connected with an undifferentiated cell syncytium, mesenchymal in nature. These undifferentiated reticular cells are large, stellate, or spindle shaped and have an abundant cytoplasm and a pale, oval nucleus. They are not phagocytic in character and possess unrestricted potentialities for differentiation. The lymphatic sinuses of the lymph nodes are lined with specially differentiated reticular cells which have been termed by Siegmund (1925) littoral cells. These cells are phagocytic and are entirely different from the endothelial cells lining ordinary blood and lymph vessels. From these fixed littoral cells clasmatocytes and the monocytes of the circulating blood are derived; these cell types are not only closely related, but are indistinguishable from each other. Their outstanding characteristic is their phagocytic property. In the germinal center of lymph follicles, lymphocytes are formed from the reticular cells. The immediate descendants of the reticular cells appear as lymphoblasts. The latter are the mother cells of the mature small lymphocyte. In this line of differentiation the phagocytic properties are lost and the resulting cells no longer store vital dyes. Further differentiation is restricted though lymphocytes may give rise to plasma cells as a result of unknown stimuli.

True mesenchymal reticulum is found in the malpighian corpuscles of the spleen, in bone marrow, and as undifferentiated cells of the connective tissue as well as in lymph nodes. In these locations also the reticular cells possess the ability to differentiate into the various described cell types.

Adhering to Gall and Mallory's general outline, but substituting some of their unfamiliar terms with those used by the Lymphatic Tu-

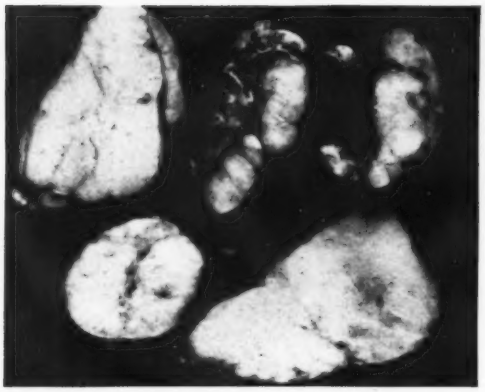

Fig. 3. Axillary lymphocytoma consisting of 5 nodes in 28 year old male. Removal of all tumors and postoperative radiation 8 years ago. Patient is living and well at present.

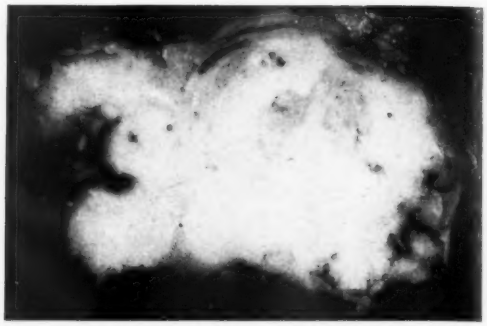

Fig. 4. Breast with large lymphoblastoma in 31 year old female. Metastases to axillary and abdominal nodes at time of admission. In spite of intensive radiation therapy, death occurred 3 months after admission.

mor Registry (Callender), I divided my material of primary lymphoid tumors into 8 groups. The number of cases encountered in this survey of 130 malignant lymphomas were as follows:

	Cases
1. Reticulocytoma	16
2. Giant cell reticulocytoma	5
3. Monocytoma	2
4. Hodgkin's disease	26
5. Lymphoblastoma	44
6. Lymphocytoma	34
7. Follicular lymphoma	2
8. Plasmocytoma	1
Total	130

In our experience, most malignant lymphomas fall into four groups, namely reticulocytoma, Hodgkin's disease, lymphoblastoma, and lymphocytoma. The percentage of the other four groups we found varies between 0.8 and 3 per cent.

Tumors composed of highly undifferentiated reticular cells are called stem cell lymphoma by Gall and Mallory, while we prefer the term of the Registry, reticulocytoma. Tumors made up of more mature phagocytic cells corresponding to littoral cells, clasmatocytes, and monocytes are designated as clasmatocytic lymphoma by Gall and Mallory, but as monocytoma by us. The group of tumors called Hodgkin's sarcoma by Gall and Mallory is apparently the same which Foot calls pleomorphic lymphosarcoma and for which we propose the term giant cell reticulocytoma. While there are authentic cases reported in which Hodgkin's diseases after a comparatively benign course becomes transformed into a rapidly progessive tumor, in our material the cases of giant cell reticulocytoma have shown their characteristic clinical and morphologic behavior from the onset.

The justification of subdividing the malignant lymphomas into 8 distinct groups rests on the constancy of the cell type in an individual case. Sixteen patients of our series had biopsies on two or more occasions or specimens were available from both biopsy and subsequent necropsy. Of our 30 autopsy cases, microscopic sections of all involved organs were studied. In about 82 per cent the original histologic structure was maintained, while in only 18 per cent the lesion became less differentiated. This degree of dedifferentiation must be expected in any group of malignant tumors followed over a longer period of time. The occasional transition from one form to another supports the view that these tumors are essentially of common origin, but does not invalidate the practical application of Gall and Mallory's classification.

CLINICAL OBSERVATIONS

Incidence. In comparison with other types of cancer, malignant lymphoma is not common. Between January, 1925, and December, 1945, 699 lymphoid tumors were submitted to our laboratory for histologic diagnosis, of

Fig. 5. Mediastinal lymphoblastoma compressing trachea and both main bronchi. Sudden death by suffocation. X-ray therapy may prevent sudden death in these inaccessible tumors; however, life expectancy of different tumor types is seldom prolonged by radiation.

Fig. 6. Intrapulmonary malignant lymphoma. Surgical removal of entire lobe eradicated the tumor, as shown by autopsy.

which 234 proved to be malignant lymphomas. They represented less than 5 per cent of all cancers examined during the 21 year period. The average number of malignant lymphomas seen in our laboratory during an average year is therefore less than twelve. Our material came from 57 surgeons and the largest number of lymphoid tumors submitted by a single surgeon was 18, while 53 physicians had only one case each.

Age. As the age of onset we have listed the age at which the first relevant symptom was noted. For the entire group the average age was 44.7 years, about 10 years lower than that for the epithelial types of cancer (53.8 years). The average age was 5 years higher in females (45.5 years), than in males (40.8 years). In general, malignant lymphoma is rare before the age of 20 years and after the age of 70. Our youngest patient was 4 months old (lymphoblastoma), and our oldest 84 years (monocytoma).

While in Gall and Mallory's series, Hodgkin's disease had a tendency to appear nearly a decade earlier than any other form of lymphoma, in our material the age of patients with Hodgkin's disease was only slightly lower than in the entire series, namely 42.3 years. The most common period of life when malignant lymphoma became evident was the fourth and fifth decades. Two types, lymphoblastoma and lymphocytoma, occurred in the first two decades with significant frequency, 14 and 10 per cent, respectively. Below the age of 40 there were 23 per cent of reticulocytomas and 25 per cent of follicular lymphomas.

Sex. It is generally stated in the literature that malignant lymphomas show a predilection for the male sex. Gall and Mallory found a definite predominance of men over women (2.2 to 1), Sugarbaker and Craver reported

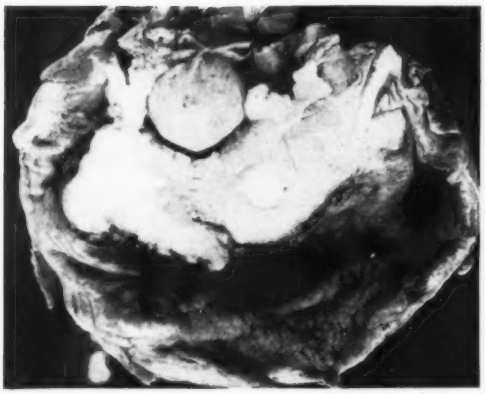

Fig. 7. Resection of stomach with primary Hodgkin's disease in 60 year old male. Complete removal of disease. No other foci found at autopsy.

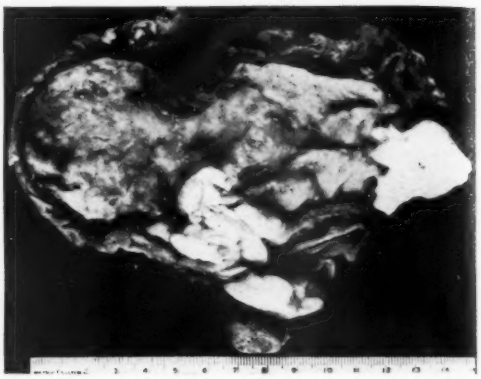

Fig. 9. Surgical specimen of giant reticulocytoma of cecum in 67 year old female; no postoperative radiation. Clinical cure since operation 6 years ago.

the same characteristic sex distribution, namely a ratio of about 7 to 3. In our own material, on the other hand, the frequency was found to be almost equal, namely 3 males to 2 females.

Primary site. Cutler states that in cases in which clinical examination discloses cervical lymph nodes invaded by lymphosarcoma, the presence of a primary lesion in the pharynx or nasopharynx should be suspected, and Coutard advises that these areas should be irradiated even when a primary focus cannot be demonstrated. In our material, which includes complete autopsy studies in 30 cases, an extranodal primary focus of the disease could be demonstrated in only one third of all cases. In 26 cases the primary focus could be reasonably assumed to arise in one of the cranial structures with the tonsils and nasopharynx as the most common sites. In 19 cases the disease arose apparently in the gastrointestinal tract (stomach, 5; ileum, 4; appendix, 2; rectum, 8 cases). In the remaining 6 cases, primary sites were widely scattered, i.e. in bone, thymus, lung, ovary, and skin.

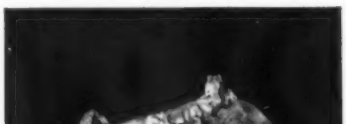

Fig. 8. Lymphocytoma of jejunum in 53 year old female. Resection was not followed by radiation. No recurrence or other manifestations of disease in following 7 years.

Two thirds of the entire series never had what could be supposed to represent an extranodal primary focus. In these the first and only subsequent evidence of disease was confined to lymph nodes until widespread dissemination took place. Our own experience therefore conforms with that of Sugarbaker and Craver that malignant lymphoma is a disease which in the majority of cases begins, and runs its early course, in the lymph nodes alone.

The site of the first lymph node involvement is of interest. In 40 per cent of the cases the lymph nodes of the neck were first involved, the axillary nodes in 9 per cent, the inguinal glands in 13 per cent, and the abdominal nodes in 4 per cent. Mediastinal nodes were enlarged in 8 per cent. In less than 2 per cent of the patients the disease appeared to involve almost the entire node system simultaneously.

TABLE I.—FIVE YEAR SURVIVALS AFTER RADICAL SURGERY WITHOUT RADIATION

No.	Age	Sex	Location	Histologic type	Follow-up
1		M	Tonsil	Reticulocytoma	Living and well, 20 yrs.
2	5	F	Jaw	Reticulocytoma	Living and well, 10 yrs.
3	67	F	Cecum	Giant cell reticulocytoma	Living and well, 6 yrs.
4	69	M	Inguinal	Hodgkin's disease	Living and well, 9 yrs.
5	53	F	Jejunum	Lymphocytoma	Living and well, 7 yrs.
6		M	Neck	Lymphocytoma	Living and well, 12 yrs.
7	9	F	Appendix	Lymphocytoma	Living and well, 5 yrs.
8		F	Skin (breast)	Lymphocytoma	Living and well, 7 yrs.
9		F	Anal	Lymphocytoma	Living and well, 6 yrs.
10	26	F	Supraclavicular	Lymphocytoma	Living, diseased, 9 yrs.
11	40	M	Neck	Lymphocytoma	Living and well, 15 yrs.
12	34	F	Appendix	Lymphocytoma	Living and well, 5 yrs.
13	27	M	Skin (shoulder)	Hodgkin's disease	Living and well, 13 yrs.
14		M	Anal	Lymphocytoma	Living and well, 11 yrs.
15		F	Groin	Lymphocytoma	Living and well, 8 yrs.
16	28	M	Axilla	Lymphocytoma	Living and well, 8 yrs.
17	34	M	Tonsil	Lymphoblastoma	Living and well, 7 yrs.
18		F	Neck	Lymphoblastoma	Living and well, 7 yrs.
19	61	M	Gum	Plasmocytoma	Living and well, 6 yrs.
20		F	Uterus	Lymphocytoma	Living and well, 6 yrs.
21	61	F	Anal	Lymphocytoma	Living and well, 5 yrs.
22	37	M	Neck	Hodgkin's disease	Living and well, 14 yrs.
23		F	Tonsil	Lymphoblastoma	Living and well, 12 yrs.
24	14	F	Thigh	Lymphoblastoma	Living and well, 7 yrs.
25		M	Inguinal	Lymphocytoma	Died, coronary, 5 yrs.
26	30	F	Neck	Hodgkin's disease	Died of disease, 10 yrs.
27	21	M	Neck	Lymphoblastoma	Died, 7 yrs.
28	35	M	Neck	Lymphoblastoma	Died, 4 yrs. 11 mos.
29		M	Neck	Follicular lymphoma	Died, 5 yrs. 8 mos.
30	25	M	Neck	Lymphocytoma	Living and well, 8 yrs.

In addition to the primary sites of involvement, numerous organs may subsequently become involved either as a result of lymphatic or hematogenous metastasis or by direct extension. The spleen was palpable in 23 per cent of our cases, liver enlargement was recorded in 6 per cent. Roentgenologic evidence of infiltration of lungs and pleura was present in 21 cases. Metastatic involvement of the skin occurred in 16 per cent and of the bones in 12 per cent.

Evidence of presumably secondary foci in the gastrointestinal tract was obtained in 27 cases. The rapidity with which lymphoma advances is readily understood when one considers that the average duration of life from onset of the disease until death was only 26.7 months.

Systemic symptoms. Chill, fever, weight loss and weakness rarely appeared before the disease had become far advanced. The general mildness of the symptoms early in the disease is evidenced by the fact that the average interval between first symptoms and hospital admission was 10.3 months. Temperature of 101 degrees and higher occurred at some time during the course of the disease in 40 per cent of the lymphocytomas and 42 per cent of the lymphoblastomas. In 55 per cent of Hodgkin's disease intermittent fever was recorded. This

type of fever was also frequent in giant cell reticulocytoma.

Blood findings. In contradistinction to Hodgkin's disease in whom anemia usually develops early (11%), the other types of lymphoma maintained good hemoglobin values for some time. On admission 61 per cent of our patients showed hemoglobin readings above 80 per cent and only 36 per cent of the cases had less than 70 per cent hemoglobin. As a result of advancing disease very definite blood changes took place. Only 32 per cent of the patients at this time had hemoglobin values higher than 70 per cent. In 16 per cent of the higher series the red cell blood count was less than three million. Profound anemia was recorded most often in lymphoblastic and lymphocytic types (15 and 11%, respectively) associated with leucemia.

A leucocytosis exceeding 12,000 per cubic millimeter on admission was found in 13 per cent of the lymphocytoma cases and in 10 per cent of lymphoblastomas. The same count was noticed in 11 per cent of Hodgkin's disease. Leucopenia with white cells numbering less than 5,000 cells per cubic millimeter was noted in about 20 per cent of lymphoblastoma and lymphocytoma and half as often in Hodgkin's disease. Monocytes in excess of 10 per cent were recorded in all cases of monocytoma and in some cases of Hodgkin's disease. In the latter, eosinophilia was not a prominent feature. Atypical cells, either unidentified or blast forms appeared in the peripheral blood of 15 per cent of the cases of lymphoblastoma and 13 per cent of those with lymphocytoma. In the other subgroups these abnormal cells were infrequent.

Blood pictures characteristic of leucemia occurred at some time during the course of the disease in 26 per cent of the cases with lymphocytoma and in 15 per cent of those with lymphoblastoma. They were absent in reticulocytoma and infrequent in the remaining types. Individual patients showed true leucemia at intervals, then subleucemic or aleucemic blood pictures. Of the patients with positive blood findings 13.2 per cent were nonleucemic when first observed, but developed leucemia later in the course; 17 per cent were leucemic at the initial observation but showed normal blood pictures prior to death, and 11 per cent were leucemic at the beginning and at the end of the disease, but were nonleucemic in the interval. In only one half of the leucemic patients was the blood picture entirely constant throughout the course of the disease. Of the patients in whom a leucemic or subleucemic picture was superimposed, none survived the 5 year period following biopsy. The duration of disease in these cases varied between 6 weeks and 4 years, its average being 15.1 months against 26.7 months for the entire series.

DURATION OF DISEASE

The duration of the disease depends to a surprising degree on the cytologic character of the underlying lesion. Four types of malignant lymphoma, namely lymphoblastoma, reticulocytoma, giant cell reticulocytoma and monocytoma offer a relatively poor prognosis with an average duration from 3.3 to 11.8 months, lymphocytoma and Hodgkin's disease run a comparatively slower course with averages of 36 and 38 months, while follicular lymphoma and plasmocytoma offer a much better outlook, lasting in the average 4.8 and 4.3 years, respectively. For the entire series of lymphoma, the average duration was 26.7 months. In even the most malignant types occasional instances of unusually long survival are met. These are least frequent in lymphoblastoma, monocytoma, and giant cell reticulocytoma. While only one giant cell reticulocytoma, 3 reticulocytomas, and 7 lymphoblastomas survived longer than 5 years, there were 17 lymphocytomas who did not show any sign of the disease 5 years and longer following operation.

The group prognosis is altered definitely by the presence of blood findings characteristic of leucemia. Patients with leucemia have a life expectancy of about 1 year less than those without leucemic manifestations. A less important factor in our series was the age of the patients at the onset of the disease; only in lymphoblastoma and Hodgkin's disease was the life expectancy shorter in the few cases which occurred before the age of 10 years.

Of all 130 patients, 32, or 24.6 per cent, have survived 5 years or longer. Ten per cent

of our patients survived eight years or more. Twenty-three, or 17.2 per cent, of the entire series are apparently cured, 7 died more than 5 years after treatment was begun and 2 are living with active disease still present. The longest duration recorded in our series was 20 years, the patient still being alive after removal of a reticulocytoma involving a tonsil.

TREATMENT

In general, malignant lymphoma is extremely radiosensitive, and it is not surprising to observe a bulky tumor mass regress to half its size after a few days of treatment and completely disappear within a week (Sugarbaker and Craver). In occasional cases in which large masses are situated in vital locations inaccessible to surgical intervention—for instance intrathoracic tumors—radiation may be life saving and may avert sudden death. On the other hand, most observers (Minot and Isaac, Sugarbaker and Craver) agree that roentgen therapy does not seem to prolong the average duration of life.

Failure to respond initially to x-ray therapy was rare in our cases of Hodgkin's disease, follicular lymphoma, and lymphocytoma, while more than one half of the reticulocytomas and 40 per cent of the lymphoblastomas failed to show any evidence of improvement following irradiation.

Only 2 of 40 patients survived the 5 year period following irradiation alone after the diagnosis had been made by biopsy. One patient had a lymphoblastoma, the other a lymphocytoma.

Since x-ray treatment has become the standard treatment for malignant lymphoma once the diagnosis has been established, a comparison of patients treated in this manner with those who have been treated solely with surgery is extremely difficult.

The pessimistic view that surgery as a therapeutic measure in malignant lymphoma is contraindicated presumably on the basis that the disease is essentially systemic is contrary to our experience. First it is noteworthy that 10 per cent of our autopsy cases certainly were not systemic in character but showed single localized lesions accessible for surgical excision. Second, the long survivals in our series following operation suggest that in certain cases of malignant lymphoma with localized lesion patients may be treated more successfully by surgical procedure than by any other means.

Surgical therapy was initially employed in 67 cases with the intention of effecting a cure and often in ignorance of the true nature of the tumor. Of the 63 patients who survived the operation 21 received no other form of therapy, while 42 received postoperative external radiation regardless of the absence of clinical symptoms.

Of the 21 patients who underwent surgical operations and who did not receive radiation therapy 12 survived 5 years or longer and none shows at present any evidence of disease. In this group the following types of malignant lymphoma were represented: 2 reticulocytomas, 1 giant cell reticulocytoma, 1 Hodgkin's disease, and 9 lymphocytomas.

In 40 instances, radical removal of a single focus of disease was followed by adequate radiation. Eighteen of the 40 patients survived and 9 are at present without clinical evidence of the disease. There were 6 lymphoblastomas, 7 lymphocytomas, 1 follicular lymphoma, 1 plasmocytoma, and 2 Hodgkin's diseases in this second group.

From these observations it must be concluded as long as malignant lymphoma is confined to an accessible single mass, that there is an excellent chance for obtaining a cure by complete removal of the primary focus.

CONCLUSIONS

1. A comparative clinical-pathologic study of 130 cases of malignant lymphoma is reported.

2. Following Gall and Mallory's cytologic classification 8 types of malignant lymphoma were distinguished corresponding to different degrees of differentiation of their component cells.

3. There was a close correlation between the histology and life expectancy of the different subgroups.

4. The average duration of disease was found to be 26.7 months for the entire series. It varied in the different histologic types between 3 months and 4.8 years.

5. Due to its striking initial effect on lymphoma, radiation therapy may occasionally save a life, when the tumor is located in a vital part of the body, inaccessible for surgery, but it will seldom prolong the life expectancy inherent to the histologic type of lymphoma.

6. Early surgical removal of a primary focus of disease offers the best chance of cure, in malignant lymphoma. In our entire series 24.6 per cent of the patients survived 5 years or longer regardless of postoperative radiation. In 21 patients with a single primary focus, radical surgery alone was used and 12 of the 21 patients survived from 5 to 20 years.

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DIGESTION OF LIVING TISSUE BY THE HYPERACID STOMACH

An Experimental Study

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IN a recent publication we showed that living autogenous organs and tissues of all sorts are completely digested in from 1 to 6 weeks when they are deeply implanted in the canine stomach. Those experiments were carried out on dogs with normal gastric secretions. In the present investigation we have repeated the experiments, using the same technique of implantation, but we have given these animals daily postoperative injections of histamine in order to study the effects of hyperacidity upon the process of autodigestion.

Sixty-six healthy adult dogs were used. Under pentobarbital sodium anesthesia, with aseptic technique, various organs and tissues of the body were implanted through large windows, usually in the anterior wall of the stomach. Care was taken not to compromise the circulation of the implants. Beginning 24 hours after operation, each animal received daily intramuscular injections of histamine dihydrochloride. The histamine was mixed with beeswax and mineral oil after the technique of Hay, Varco, Code, and Wangensteen. Uniform daily doses of 30 milligrams of histamine base were administered irrespective of the weight of the dogs.

The animals were observed closely following operation. Food ("purina" dog chow) and water were allowed *ad libitum*. Periodic measurements were made of weight, temperature, hematocrit, hemoglobin, blood cell counts, and plasma proteins. At suitable intervals the implants were explored surgically or the animals were sacrificed and examined, blocks being cut for microscopic study. These examinations were usually made 24 hours after the last injection of histamine. At the time of implantation, before the animals had received histamine, and subsequently whenever the stomach was opened at operation or autopsy, samples of fasting gastric contents were secured for analysis. The dogs used in these experiments averaged 19.3 units of free acid and 55.1 units of combined acid before histamine was injected; after histamine the samples averaged 91.4 units of free acid and 33.1 units of combined acid.

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EXPERIMENTS

1. Digestion of living omentum. The corrosive effect of hyperacid gastric juice upon the omentum was pronounced. Characteristic fibrosis and granulation tissue response occurred but were ineffectual barriers to the digestive process. Omental patches covering large gastric windows had irregular necrotic craters after 2 weeks, and one such patch perforated on the twentieth day with resultant general peritonitis. Large tongues of omentum implanted deeply in the lumen of the stomach were more rapidly digested in these dogs than were similar preparations in normal animals.

2. Digestion of living intestine. Implants of intact jejunum, appendix, and cecum were quickly digested by the hyperacid stomach. Two out of 6 animals died within 24 hours of hemorrhage from the rapidly eroding intestinal wall. Perforation of the implant usually occurred in less than 1 day, and much of the implant had disappeared entirely by the eighth or tenth day. Histologic changes were observed similar to those previously reported for normal dogs, but the process of inflammation, necrosis, and digestion appeared to be far more acute in the present series.

3. Digestion of living organs. An implanted lobe of liver showed partial erosion after 3 days and digestion nearly to the level of the gastric wall within a week. In normal dogs complete

digestion of the hepatic implant was not obtained until the end of the fourth week.

The gall bladder was implanted in 3 hyperacid dogs. After 24 hours (that is, 24 hours after histamine was started), the gall-bladder wall had perforated and was partly digested; after 3 days the implanted portion had almost entirely disappeared leaving a large ragged fistula between the stomach and the remainder of the gall bladder.

The tail of the pancreas was implanted in 2 dogs. In both instances complete digestion of the implant occurred within 3 days.

The lower pole of the spleen was successfully implanted in 3 animals. This organ was likewise digested rapidly by the hyperacid stomach, partial digestion occurring in 2 days and complete digestion to the level of the stomach wall after 3 days. A similar degree of digestion was not observed in normal animals before the nineteenth postoperative day.

The superior pole of the left kidney was satisfactorily implanted in 3 dogs. All of the implants showed relatively rapid digestion, as compared with digestion of similar implants in normal dogs. One animal, sacrified on the nineteenth day, showed loss of the entire upper pole with exposure of the calyces to gastric juice.

4. Digestion of living connective tissue. Cartilaginous ends of ribs were fully digested away after 3 days of hyperacidity (4 days after implantation).

Pedicle skin flaps from the anterior abdominal wall likewise suffered relatively rapid digestion, as did free skin grafts growing on intra-abdominal serosal surfaces.

When large gastric windows were sewed to the parietal peritoneum of the anterior abdominal wall, progressive erosion of the tissues occurred. These ulcerations eventually extended through muscle and fascia forming abscesses. One dog died on the fourth postoperative day with a large abscess beneath the anterior rectus fascia. Another dog died on the sixth postoperative day with a subcutaneous abscess which extended to the axilla.

5. Digestion of living gastric tissue. Artificial "ulcers" were produced in the stomach by cutting away round or oval areas of mucosa. The defects exposed the outer layers of the stomach wall to the digestive action of the strongly acid gastric juice. These lesions all showed progressive erosion of both mucosal margins and "ulcer" base. One dog died of perforation and peritonitis 3 days after operation and 2 days after the histamine was started. Another dog which was sacrificed on the seventh postoperative day was about to perforate.

Pedicle flaps of gastric wall turned into the lumen of the stomach, as described in our previous article, were digested in 3 to 6 days. When these flaps were denuded of mucosa at the time of implantation, complete digestion occurred in less than 3 days.

OBSERVATIONS

Daily injections alone of 30 milligrams of histamine base will cause spontaneous ulcerations in the previously healthy stomach and duodenum. Hay and his associates found that of 12 dogs so injected 8 developed duodenal, and 3 developed gastric, ulcers. These animals received an average of 24 doses of histamine, although 1 dog had a large gastric ulcer and a nearly fatal hemorrhage after only 4 injections. Another died after 7 injections of multiple perforated duodenal ulcers. Other investigators have obtained similar results. Crandall in this laboratory injected 10 dogs (4 normal dogs, 4 with Finney pyloroplasties, and 2 with gastroduodenostomies) and obtained ulcers—gastric, duodenal, or both—in all of them. The duration of histamine therapy in this control series was from 8 to 44 days. It was not determined how soon the ulcers developed, but one of the dogs died on the eighth day as a result of a perforated duodenal ulcer and peritonitis.

In our larger series, where the animals had operative implants and subsequent injections of histamine, there were only 5 instances of independent ulcer formation at a distance from the implant. This relatively small incidence of ulcer production is explained by the short duration of the experiments. Our dogs died or were sacrificed, on the average, 4.9 days after histamine therapy was instituted. Duodenal ulcers were observed in 4 dogs which had received histamine 5, 5, 4, and 3 days, respectively, and 1 dog which had received histamine

injections for only 3 days showed both gastric and duodenal ulcers. None of them had perforated. On the other hand, 2 dogs which had received histamine for 19 days showed no evidence of spontaneous ulceration.

Pronounced deterioration of health was noted in about two-thirds of our animals. Loss of appetite was a constant feature. Weight loss for the entire group averaged 2.77 per cent of the original body weight per day. Hair lost its gloss and was shed freely. Vomiting was conspicuous in 5 cases.

Most of the animals developed a moderate degree of anemia. Hematocrit determinations for the entire series fell from an average of 47.9 to 38.0; hemoglobin from 17.2 grams to 13.7 grams; and red cell counts from 6,330,000 to 4,824,000. Total plasma proteins showed relatively little change, however, the preoperative average being 6.36 grams as compared with a final average of 6.18 grams. Gross bleeding from the implant was a common finding; 9 of the animals were seen at autopsy to have had large, perhaps fatal hemorrhages into the gastrointestinal tract.

In our previous report on digestion of living tissue by the normal stomach it was observed that "a number of our animals appeared toxic, some were quite ill in fact, during the period of necrosis and digestion of the implants; but these animals recovered full health after the necrotic tissue had disappeared. This phenomenon was observed particularly after implantation of intestines, gall bladder, and solid organs." This "toxicity" appeared to be even more pronounced in the present series. Elevation of temperature was frequently seen. The white blood cell count rose from an average of 10,020 to 19,015.

Histologic examination of the margins of implants showed that proliferation of gastric epithelium was feeble or absent, and in some instances there was progressive autodigestion of the gastric wall and extension of the area of erosion. This picture was in striking contrast to that which was seen in the normal stomach where vigorous epithelial proliferation across the base of the implant was the general rule.

SUMMARY AND CONCLUSIONS

An experimental study has been carried out in which living autogenous organs and tissues of various sorts were implanted in the stomachs of dogs. Following implantation the animals received daily injections of histamine in beeswax in order to produce a high degree of hyperacidity. Results of these experiments have been compared with those of a similar series of implantations in stomachs not stimulated by histamine injections.

The implants were all digested. The rate of digestion by the hyperacid stomach greatly exceeded that shown by the normal stomach. Tissue reactions to the corrosive process were also more violent.

Only a small proportion of the animals receiving histamine developed spontaneous ulcers at a distance from the implant, presumably because the experiments were too acute. In a control series, 10 dogs which received more prolonged histamine therapy all developed gastric or duodenal ulcers.

Most of the dogs receiving histamine showed deterioration of general health.

Some of the implants bled grossly during the process of digestion, and virtually all of the animals with implants developed at least a moderate degree of anemia.

Evidences of toxicity were pronounced during the period of digestion of the implants.

No living tissue, not even gastric epithelium itself, appeared to be immune to digestion by the hyperacid stomach. Fibrosis and granulation tissue occurred in some of the implants, but seemed to be ineffectual barriers to the corrosive action of very acid chyme.

This investigation supports the results of our previous study and justifies the general conclusion that living organs and tissues of all sorts are susceptible to gastric digestion, and that hyperacidity increases the rate of that digestion.

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ADOLESCENT PRIMIGRAVIDA

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LABOR at either extreme of the woman's reproductive life is considered by many physicians to be fraught with additional hazards. That this is true in the elderly primigravida has been stated by numerous authors. The young primigravida, however, receives little attention in our present day texts. Greenhill (2) in the eighth revision of Dr. DeLee's text devotes the following paragraph to its consideration: "Labor in young primipara shows little variation from the usual. Eclampsia, premature delivery, atonia uterii, and breech presentation are slightly more frequent and there is a slight increase in perineal lacerations and fetal mortality. Labor is shorter, somewhat easier, and there is less hemorrhage. The pelvis is larger than one would expect." If this be true, there is no cause for alarm when an adolescent mother presents herself for prenatal care. Labor should be conducted with the same precaution and alertness as is customary but meddlesome midwifery, under the guise of assistance, precipitated by the belief that catastrophe awaits the young mother, is to be avoided. That we might aid the accoucheur in maintaining his equanimity while practicing that greatest of virtues necessary for the successful management of childbirth, namely, watchful expectancy, this study was undertaken.

MATERIAL

At St. Vincent's Infant and Maternity Hospital, a unit of the Department of Obstetrics and Gynecology of Loyola University Clinics, the percentage of adolescent primigravida is high due to the number of unwed mothers cared for. This circumstance afforded an excellent opportunity to assemble 200 consecutive cases of primigravida 17 years of age or under (Table I).

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Read at the Twenty-fourth Annual Fall Clinical Conference of the Kansas City Southwest Clinical Society, Kansas City, Missouri, October 7, 8, 9, 10, 1946.

TABLE I.—AGE INCIDENCE

Age groups years	No. cases
12	3
13	3
14	6
15	27
16	66
17	95
Total	200

The majority of these patients report to the prenatal clinic early in their pregnancy and during the last 2 lunar months are secreted in the institution; their prenatal care must, therefore, be considered adequate. The deliveries are managed by the resident obstetrician under the supervision of the authors. It is our custom to perform mesiolateral episiotomy in all cases, and the second stage of labor is terminated by elective outlet forceps operation. Pudendal block or caudal anesthesia was employed in all cases. The third stage of labor is managed by administering intravenous ergotrate with the delivery of the anterior shoulder.

TWELVE YEAR OLD GROUP

Although precocious pregnancy reports appear in the literature they are too rare to merit consideration at this time. The youngest patients in our group as shown in Table II were 12 years of age.

Harris, in 10,000 cases at Johns Hopkins, had only 2 cases of pregnancy in patients of this age. Williams had 3 cases of pregnancy in 12 year old patients. This infrequency occurred in spite of the fact that their clinic was in an area populated heavily with negroes who presumably mature at an earlier age. All of our patients were white. The average length of labor for our 3 patients was 13 hours, 33 minutes for the first stage, 62 minutes for the second stage, and 7 minutes for the third stage. There were no complications, mortalities, nor morbidities among these 12 year old mothers.

TABLE II.—DURATION OF LABOR

Twelve year old group (3 cases)

Case No.	First stage		Second stage	Third stage
	hrs.	min.	min.	min.
1	9	30	36	4
2	13	30	60	10
3	17		92	8
Average	13	33	62	7

There were no complications, mortalities nor morbidities among these 12 year old patients.

The average length of labor for the first stage was 6 hours and 7 minutes, for the second stage 1 hour and 5 minutes. The third stage averaged 52 minutes. In 1 case the cord prolapsed and in spite of the fact that the infant was resuscitated, it died 12 hours later of respiratory complications. In the patient having a 2 hour, 7 minute third stage, a manual removal of the placenta was done.

THIRTEEN YEAR OLD GROUP

In Table III are listed 3 patients in the 13 year age group.

TABLE III.—DURATION OF LABOR

Thirteen year old group (3 cases)

Case No.	First stage		Second stage		Third stage	
	hr.	min.	hr.	min.	hr.	min.
1	11		2	41		5
2	3			5		25
3	6	10		23	2	7
Average	6	7	1	5		52

In this series 1 infant expired 12 hours after delivery which was complicated by a prolapse of the umbilical cord.

FOURTEEN YEAR OLD GROUP

In the 14 year age group (see Table IV) there were 6 patients with an average length of labor of 31 hours and 50 minutes for the first stage, 42 minutes for the second stage, and 7 minutes for the third stage. The average time of the first stage was increased because of 1 case of prolonged labor. The first stage in this instance lasted 66 hours; the labor terminated spontaneously with the birth of a living infant; the episiotomy, however, became infected. There was 1 stillbirth of a monstrosity.

TABLE IV.—DURATION OF LABOR

Fourteen year old group (6 cases)

Case No.	First stage		Second stage		Third stage
	hr.	min.	hr.	min.	min.
1	10	30	1	10	11
2	66		1	39	6
3	7			20	5
4	15	20		15	3
5	4			23	15
6	7	30		30	3
Average	31	50		42	7

In this series there was 1 stillbirth of a monstrosity and 1 infected episiotomy following the case of prolonged labor.

FIFTEEN YEAR OLD GROUP

In the 15 year age group of 27 cases the individual length of labor is not listed but Table V gives the average length for each stage.

TABLE V.—DURATION OF LABOR

Fifteen year old group (27 cases)

Total No. cases	Average length first stage	Average lengthsecondstage	Average length third stage
27	10 hr. 13 min.	46 min.	16 min.

COMPLICATIONS

Prolonged labor	2 cases
Neonatal death	1 case
(Congenital heart defect 8th postnatal day.)	
Morbidities	2 cases
Retained placenta postpartum hemorrhage	1 case

The average for the first stage was 10 hours, 13 minutes; for the second stage, 46 minutes; and for the third stage, 16 minutes. There were 2 cases of prolonged labor each with a first stage of 28 hours. One necessitated a forceps rotation because of a transverse arrest; the other terminated spontaneously. The 1 morbid case in this group was due to an upper respiratory infection; the other was unclassified. There was 1 neonatal death, the infant succumbing on the eighth postpartum day because of a congenital heart defect. One patient had a retained placenta which was removed manually after 3 hours and 43 minutes. The blood loss amounted to 950 cubic centimeters.

SIXTEEN YEAR OLD GROUP

Labor in the 66 patients in the 16 year age group averaged 13 hours, 26 minutes for the

first stage, 48 minutes for the second, and 11 minutes for the third stage as shown in Table VI.

TABLE VI.—DURATION OF LABOR

Sixteen year old group (66 cases)

Total No. cases	Average length first stage	Average lengthsecondstage	Average length third stage
66	13 hr. 26 min.	48 min.	11 min.

COMPLICATIONS

Prolonged labor	6 cases
Pre-eclampsia	6 cases
Postpartum hemorrhage	3 cases
Morbidity	4 cases
Premature separation of the placenta	1 case
Intrauterine asphyxia	1 case
Midforceps delivery	2 cases

There were 6 cases with a first stage over 24 hours, our criterion for a prolonged labor. The longest first stage in this group was 41 hours and the remaining prolonged cases ran but a few hours over the accepted limit for normal. Midforceps operation was performed in 2 instances; in 1 case after 6 hours and 46 minutes in the second stage without progress; in the other after a forceps rotation from an occiput right posterior, this being one of the prolonged labor group. Postpartum hemorrhage occurred 3 times, once in a mild pre-eclamptic with a loss of 900 cubic centimeters. In a second case apparently normal in all respects, 625 cubic centimeters of blood was lost during and at the termination of the third stage. The third patient with a labor of 2 hours, 1 hour and 7 minutes, and 18 minutes respectively for the 3 stages, lost 1300 cubic centimeters of blood. In none of these patients was it considered necessary to pack the uterus. Plasma and whole blood were given immediately, and their postpartum course was uneventful.

The 6 cases of pre-eclampsia were in patients who showed excess weight gain, edema, or an elevation of blood pressure above 140 millimeters of mercury systolic or 90 millimeters of mercury diastolic. It is our practice to segregate all such cases for special care.

The premature separation of the placenta occurred after a normal first stage of 22 hours and a second stage of 1 hour and 7 minutes. The heart tones became inaudible shortly before termination of labor which resulted in delivery of the infant and placenta simultaneously; blood loss was minimal. This infant had asphyxiated *in utero*. The 4 morbid cases were due to endometritis in 3 instances and fissured nipples in the fourth.

SEVENTEEN YEAR OLD GROUP

In the 17 year old group we have the greatest number of cases and consequently more complications. Table VII lists the complications and the average length of labor.

TABLE VII.—DURATION OF LABOR

Seventeen year old group

Total No. cases	Average length first stage	Average lengthsecondstage	Average length third stage
95	16 hr. 43 min.	1 hr. 16 min.	16 min.

COMPLICATIONS

Prolonged labor	9 cases
Pre-eclampsia	2 cases
Postpartum eclampsia	2 cases
Postpartum hemorrhage	1 case
Abruptio placenta	1 case
Polyhydramnios with an anencephalic monster	1 case
Morbid cases	6 cases
Placenta lateralis	1 case
Prolapsed cord	1 case
Stillbirths	3 cases
Midforceps delivery	1 case
Twin pregnancy	1 case
Cesarean section for disproportion	1 case

The first stage averaged 16 hours, 43 minutes; the second stage, 1 hour, 16 minutes; and the third stage 16 minutes. There are listed 9 patients with prolonged labor, who had a first stage of an average of 33 hours, all of which terminated spontaneously with live infants. There were 2 mild pre-eclamptics in this series and 2 postpartum eclamptics. One of the latter had convulsions. All recovered and had living infants. One mother had a postpartum blood loss of 1000 cubic centimeters and her uterus was packed to control the bleeding. There was 1 case of abruptio placenta at the 29th week of gestation and this resulted in a stillbirth. The patient with placenta previa lateralis was delivered vaginally of a living infant. There was 1 patient with polyhydramnios of 3,000 cubic centimeters who gave birth to an anencephalic monster; this case is listed as the second still-

birth. The third stillbirth resulted from prolapse of the cord. The 1 cesarean section in our entire group was due to cephalopelvic disproportion. The mother had a 12 hour test of labor and as a result developed an endometritis and is listed as a morbid case. The 5 other morbidities were due to mastitis, upper respiratory infection, right lower lobe pneumonia, cystitis, and 1 not classified. There was 1 set of twins in this group and in 1 case a midforceps application for transverse arrest.

COMPLICATIONS OF LABOR

Prolonged labor cases	18 or 9 per cent
First stage (average)	36 hours 41 minutes
Second stage (average)	1 hour 36 minutes
Third stage (average)	9 minutes
Delivery	
Spontaneous or outlet forceps	196
Midforceps	1
Midforcep rotations	
Occiputposterior positions	2
Transverse arrest	1
	3 or 2 per cent incidence
Cesarean section for disproportion	1 or 0.05 per cent

Routine L.M.L. episiotomies in all cases.
One case of infected episiotomy.
All were cephalic presentations.

DISCUSSION

Although there are not sufficient cases in each group to provide accurate statistical data, a summary of all the cases provides us with definite information relative to labor in the adolescent primigravida. The length of labor in all cases was somewhat shorter than what we consider normal for primipara. Spiller in studying 1400 consecutive primiparas delivered by the vaginal route agrees with DeLee, Nathanson, Dauhman, Miller, and others that the younger the mother, the shorter the labor. Our study confirms this belief. The incidence of prolonged labor in this group was 9 per cent which is higher than our incidence of 2.5 per cent for all cases. All delivered spontaneously, however, and without fetal mortality. Uterine inertia was not encountered and in no instance was it found necessary to employ drugs to stimulate uterine contraction. If allowance were made for ineffectual pains early in labor, this incidence would be lowered considerably.

Labor was terminated spontaneously by elective outlet forceps in 196 cases or 98 per cent. Forceps interference was necessary in but 4 instances and 3 of these were for purposes of rotation. This incidence of 2 per cent is within our average incidence and lower than other reports for a similar series. The 1 case in which abdominal delivery was necessary makes the incidence of cesarean section 0.5 per cent. This figure is below our incidence of 2 per cent for all cases. In the entire group few pelvic abnormalities were present and no difficulty was encountered because of lack of development of the individual. Posner and Pulver in studying 100 girls between the ages of 12 and 15 at the Harlem Hospital found deformed pelves in 17.25 per cent and their operative incidence of 12.8 per cent. Our incidence was but 2 per cent which compares with an incidence of 1.4 per cent reported by Bromberg and Brzezinski in their study of 136 primparas of 14 to 16 years of age. Our percentage of morbid cases were 6 per cent in contrast to Posner and Pulver's incidence of 22.6 per cent. Our total number of morbid cases consisted of 13 cases: 1 case of infected episiotomy, 3 of upper respiratory infection, 1 of temperature cause unknown, 4 of endometritis, 2 of mastitis, 1 of pneumonia, and 1 of cystitis. We, therefore, cannot agree with their statement that "This is a disquieting factor and shows less fitness for pregnancy in the young group."

The antepartum complications totaled 15 or 7 per cent, and postpartum complications 9 or 4 per cent. These figures are within our average for the entire obstetric service. Complications of labor consisted of: 8 cases of preeclampsia, 2 of prolapsed cord, 2 of abruptio placenta, 1 of placenta previa lateralis, 8 of postpartum hemorrhage, 1 of postpartum eclampsia (convulsions), 1 of eclampsia, 1 of cephalopelvic disproportion, a total of 24 cases or 12 per cent.

The uncorrected infant mortality was 4.5 per cent; of these, 2 or 1 per cent were neonatal deaths. The 1 infant expired 12 hours after delivery complicated by a prolapsed cord. The second succumbed on the 8th postpartum day of a congenital heart defect. The 7 stillbirths, an incidence of 3.5 per cent, were

due to monstrosities in 2 instances, prolapsed cord in 1, abruptio placenta in 2, eclampsia in 1, and the other cause was undetermined.

Perineal laceration and injuries were not experienced in our series because of our custom of doing routine episiotomy. In only 1 case was it necessary to place a stitch in the cervix to repair a laceration. Postnatal follow-up was satisfactory in all cases.

SUMMARY AND CONCLUSIONS

1. Two hundred case histories of primigravidas between the ages of 12 and 17 have been reviewed and the results tabulated.

2. Labor was found to be somewhat shorter in all three stages and terminated spontaneously in 98 per cent.

3. The complications of labor and the puerperium were not unusual and occurred in only 24 or 12 per cent of the cases. Fifteen or 7 per cent were antepartum and 9 or 4 per cent postpartum complications.

4. The morbidity for the entire group was 13 cases or 6 per cent.

5. The infant mortality uncorrected was 4.5 per cent; 1 per cent neonatal deaths and 3.5 per cent stillbirths.

6. Cesarean section for cephalopelvic disproportion was found to be necessary in only 1 case.

7. Birth canal injuries were avoided.

8. There was no maternal mortality.

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RESULTS OF TREATMENT OF EPIDERMOID CARCINOMA OF THE ANUS AND RECTUM

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STATISTICAL studies of cases of carcinoma of the rectum have not always given separate consideration to the group with epidermoid carcinoma of the anal canal. It is obvious to anyone who has had experience with these cases that the clinical course and response to treatment of the epidermoid carcinoma group differ in many respects from those of the adenocarcinoma cases. Although these differences have been generally recognized, there has not always been a uniform opinion about what they entail. With this fact in mind a study of epidermoid carcinoma of the rectum arising in the anal canal has been made from the case records of the Palmer Memorial and Massachusetts General Hospitals.

Epidermoid carcinoma of the anus is a relatively rare type of rectal carcinoma (1). This fact is borne out by the observation that of 802 consecutive cases of carcinoma of the rectum seen at the Palmer Memorial Hospital, only 38 (4.7 per cent) were of the epidermoid variety.

It is well known that in general carcinoma of the rectum occurs in the ratio of approximately 3 men to 1 woman. Of the 77 patients who comprise this group of cases of epidermoid carcinoma, there were only 24 men as compared with 53 women. There is no satisfactory explanation for the fact that this type of tumor is apparently so much more common among women than among men.

CHARACTERISTICS OF THE TUMOR

When it comes to a consideration of the type of treatment to be used, and especially as an aid to the understanding of the course of the disease and the end-results of treatment, a knowledge of the gross condition and histological characteristics of the growth is of value.

From the Surgical Services of the Palmer Memorial and Massachusetts General Hospitals, Boston.

Size (Table I). Information concerning the size of the tumor is available in 65 of the cases. In 28 cases the growth was classified as small. In this group were put all those which were confined to the anus itself without evidence of invasion of adjacent tissues and those which were not large enough to encircle the lumen or to extend much into the rectum above. In 37 cases the growth was called large. This group included all annular tumors, all those which had invaded the surrounding tissues (perirectal fat, skin of the buttock or perineum, and vagina) or those which had extended into the upper rectum.

Invasiveness. In 58 cases the presence or absence of invasion of adjacent tissues (vagina or perirectal fat) is known. In all, there were 36 cases in which the growth had invaded the vagina or perirectal tissues.

These observations make it apparent that only about 39.4 per cent of the cases could be considered favorable insofar as the local extent of the disease is concerned (Table I).

Histological grading. In all but 6 cases these tumors were studied from the standpoint of the degree of malignancy based upon the appearance of the tissue under the microscope. Only 7 were called grade 1. In 26 cases the tumor was classified as grade 2, and in 38 cases it was considered to be grade 3.

Groin involvement. There were definite metastases to the lymph nodes of one or both groins of 18 patients at the time of the first examination. In 33 the groins were apparently not involved. In the remainder either the groins were not described or the examiner was uncertain about his observations (Table II).

METHODS OF TREATMENT

Of the 77 patients who were observed, 5 were not treated because of (1) the extremely advanced stage of the disease, (2) the excessive age of the patient, or (3) the refusal of the patient to accept the treatment which was ad-

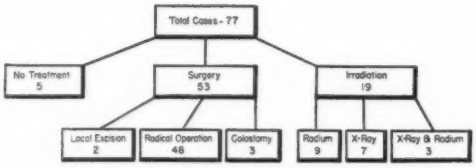

Chart 1. Types of treatment used in 77 cases of epidermoid carcinoma of the anus and rectum.

vised. Of the remaining 72 patients, 53 were operated upon and 19 were treated by irradiation (Chart 1).

Surgical cases. Of those who were operated upon, 3 with far advanced disease were given a colostomy because of intolerable obstruction, 2 had a small localized growth removed by local excision, and 48 patients were given the benefit of radical extirpation of the disease by either the combined abdominoperineal or the colostomy and posterior excision methods.

It is important to observe at this point that in only 13 of the cases in which radical surgery was employed was the growth a small one confined to the anus. In 33 the growth was large and in 23 of these it had already invaded the vagina or perirectal fat (Table III). In other words, in the majority of the cases in which surgery was employed the growth had progressed well beyond the early stages of development. This fact should be kept in mind when comparing the results with those obtained by the use of radium.

The histological grading of the tumors in these 48 cases was: grade 1—2 cases, grade 2—17, grade 3—28, undetermined—1 case. From these figures it is apparent that the majority were grade 2 or grade 3, and that more than half were grade 3.

Combined abdominoperineal excision of the rectum was used in 28 cases. In 24 the operation was performed in one stage and in 4 it was considered to be necessary to use the two stage technique (Jones method). In the remaining 20 cases a colostomy and posterior excision of the rectum was performed; in 5 in one stage and in 15 in two stages. It was possible to use the colostomy and posterior excision in such a relatively large number of cases because of the fact that the growth was low in all. It was chosen frequently because of the fact that the abdominal stage of this operation is much simpler and less upsetting to the patient than that of the combined abdominoperineal excision. This made it possible to operate successfully upon a few of the aged or otherwise relatively poor risk patients. The combined abdominoperineal method was chosen in the better risk cases or because the wide extension of the tumor made it seem that the posterior approach would be inadequate.

TABLE I.—GROSS CHARACTERISTICS OF THE TUMOR (72 TREATED CASES)

	Radiation treatment group	Surgically treated group	Total
Size			
Small	6	22	28
Large	10	27	37
Not stated	2	5	7
Local invasiveness			
Positive	10	26	36
Negative	4	18	22
Not stated	5	9	14

TABLE II.—GROIN INVOLVEMENT (AT FIRST EXAMINATION)

	Radiation treatment group	Surgically treated group	Total
Involved	7	11	18
Not involved	8	25	33
Not stated	4	17	21

Irradiation treatment cases. Irradiation by means of roentgen rays, radium alone, or both combined was used in 19 cases. Of these, 7 patients were treated by deep roentgen ray only. The remaining 12 patients were given radium. In 3 of the latter supplementary roentgen ray treatment was used. The method of treatment varied from case to case, but in the majority of the radium-treated cases interstitial irradiation with platinum needles or with gold radon seeds was used. The roentgen ray treatment was usually used only with palliation as an object and was usually not given in doses of larger than 1500 to 2500 roentgen units. Two patients only were treated heavily with doses of 5400 roentgen units and 7500 roentgen units respectively. In all 3 cases in which both forms of irradiation were used, the treatment was begun with radium and x-ray was used to treat recurrent disease or metastases to the groins.

Choice of treatment. The choice between operative and irradiation treatment was made on the basis of the merits of each case. In gen-

TABLE III.—GROSS CHARACTERISTICS OF THE TUMOR IN THE PATIENTS SUBJECTED TO RADICAL OPERATION

	Colostomy and posterior excision	Combined abdominoperineal excision	Total
Small	5	8	13
Large but not invading adjacent tissues	4	6	10
Large, invading vagina or adjacent tissues	10	13	23
Not stated	0	2	2
Total	19	29	48

eral, radical excision was used in any case in which the patient was a reasonable risk for surgery and also in all those with a growth too large or too inaccessible for radium unless it was inoperable, when roentgen ray treatment was given. In a few cases, however, the decision in favor of the use of radium was undoubtedly made because of the clinician's preference for this method in a low, fairly accessible epidermoid carcinoma of the anal canal. In the last analysis, the judgment and experience of the individual surgeon in charge were what determined the decision in each case.

RESULTS OF TREATMENT

Chart 2 shows the results of treatment in this group . Of the 77 cases of epidermoid carcinoma of the anal canal and rectum which constitute the basis of this study, the end-result is known in 75 cases. Taken as a whole, the results are discouraging especially when compared with those obtained in the adenocarcinoma group. In a very carefully followed series of cases of carcinoma of the rectum, including every patient seen by him, Dr. D. F. Jones reported 26.2 per cent of all the patients he had seen to be alive and apparently well at the end of 5 years. In the group of epidermoid carcinomas reported here only 13 patients lived 5 years or more free from disease, representing a possible 5 year cure rate of approximately 17.3 per cent of the entire group. Whether or not this relatively poor result is related in any way to the fact that in the epidermoid group an appreciable number of patients were treated by irradiation methods instead of by radical surgery is not certain. But this contention is in part substantiated by this report. It is probable that if a larger proportion of patients had been operated upon, a higher percentage of cures would have been obtained.

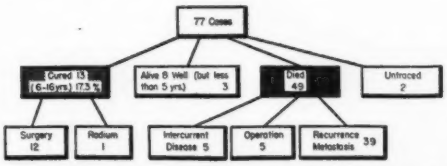

Chart 2. End-results in 77 cases of epidermoid carcinoma of the anus and rectum.

Surgical treatment. The 3 patients who were treated by colostomy alone died of their disease, but 1 survived almost 2 years.

Both of the patients who were treated by local excision of a small lesion died of local recurrence and distant metastases, one after 2 years and the other 3 years after operation.

In Dr. Jones' report based upon all his cases, including epidermoid and adenocarcinoma types, radical operation resulted in 55 per cent of 5 year cures (2). In the present series of epidermoid carcinoma of the anus and rectum, of the 48 patients operated upon radically (including both abdominoperineal and colostomy and posterior excision techniques), 12 patients lived 5 years or more without disease. If we exclude 3 patients whose operations were performed less than 5 years ago and 2 who are untraced, a 5 year cure rate of the operative cases of 28.8 per cent is observed. This should be compared with the 17.3 per cent for the group as a whole. This result might be improved if the abdominoperineal excision were used in all of the cases instead of the colostomy and posterior excision, which never results in the removal of as much of the area of lymphatic spread as the former procedure and which in Dr. Jones' experience with carcinoma of the rectum as a whole resulted in only 37.7 per cent of 5 year cures as compared with 55 per cent in the combined abdominoperineal excision group.

Chart 3 summarizes the results of radical operative excision in the 46 cases in which the end-result is known. Twelve are classified as cured. The survival period in this group varies from 6 to 16 years. In 6 of these cases the growth was large and locally invasive. In the remaining 6 cases the tumor was small, but in 2 of these there was definite evidence of invasion of adjacent tissues. In 9 of the 12 cases

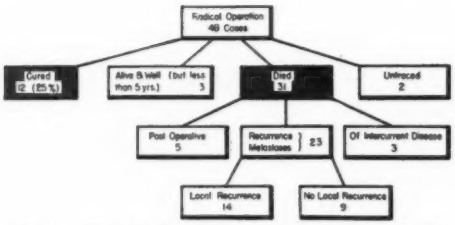

Chart 3. Results of radical surgery in 48 cases of epidermoid carcinoma of the anus and rectum.

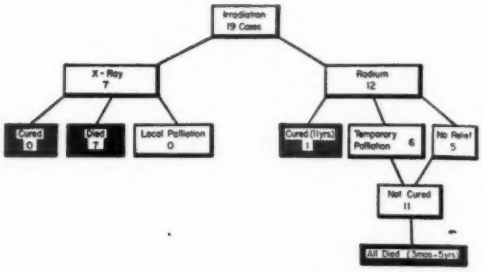

Chart 4. Results of irradiation treatment in epidermoid carcinoma of the anus and rectum.

the tumor was classified as grade 3 malignancy histologically. Eight were operated upon by the abdominoperineal method (one stage) and 4 by the colostomy and posterior excision technique (two stage). It is interesting that all those patients who were operated upon by the colostomy and posterior excision technique survived an unusually long period of time (8, 14, 15, and 16 years respectively).

Three patients are alive and apparently well less than 5 years after operation. These are not yet classified as cured.

The remaining 31 patients are dead. Among this group there were 5 operative deaths. Two of these were caused by acute small intestinal obstruction. Both occurred before the invention of the Miller-Abbott tube. In each case an enterostomy performed for the relief of the obstruction was unsuccessful. Today with the prompt use of a Miller-Abbott tube these deaths might be prevented. One patient died of pyelonephritis, another of pulmonary edema, and the fifth patient succumbed to postoperative pneumonia.

Of the remaining 23 deaths, all of which occurred in less than 5 years following radical surgical removal, there were 14 patients in whom there was a definite local recurrence of the growth, but there were 9 in whom death occurred from metastases without any sign of a local recurrence of the disease. In other words, as a result of surgery there was good local palliation; that is, freedom from recurrence in 21 cases. Twelve of these were cured and 9 died of distant metastases without local recurrence of the disease. This fact should be kept in mind when comparing the results of surgery with those of irradiation treatment.

TABLE IV.—DISTRIBUTION OF METASTASES IN 23 CASES IN WHICH THE LOCATION IS KNOWN

Inguinal nodes	16
Mesenteric nodes	5
Liver	2
Spine	2
Lungs	1

The location of distant metastases in the 23 patients who died of recurrent or metastatic disease following radical extirpation of the growth is summarized in Table IV. As one would expect, there was a high incidence of metastases to the groins in this group of cases because of the lymphatic communications which exist between the anus and the inguinal nodes (16 of 23 cases).

Irradiation treatment. Some form of irradiation treatment was used in 19 cases (Chart 4). It would be interesting and valuable to be able to say just why this method was chosen in each of these cases, but from the records this cannot always be done with certainty. An attempt was made to obtain this information from the surgeons in charge, but after the passage of several years it is often difficult to recall just what the reasoning was. Obviously some of the cases had reached the stage of local inoperability and the choice in favor of irradiation was made merely in the hope of producing some degree of palliation. This was true of the majority of the x-ray treated group, 3 of whom already had groin metastases when they were first seen. In many cases it was because the surgeon believed that as a result of either advanced age or poor general condition, the patient would not survive a radical operation. Some of these patients if seen today would undoubtedly be operated upon because of the improvements in anesthesia and general preoperative and postoperative care which have

increased the operability of all types of rectal or colon carcinoma. Some of these patients, however, were treated with radium in the belief, which seems to be held by certain surgeons, that these tumors, like epitheliomas of the skin, respond favorably to the effects of irradiation. The truth of this belief remains to be proved by those who subscribe to it. A study of this group of cases tends to lead one to believe that it is erroneous. Chart 4 summarizes the results.

Of the 7 patients who were given x-ray treatment alone, 3 were inoperable because of metastases to the groins. In each of these cases the growth was a large one, but the remaining 4 might have been operated upon with better prospect of palliation if not of cure. All 7 died. None lived more than a year. Two showed a slight temporary regression in the size of the tumor. In none was there any significant relief from pain and tenesmus. As a method of palliation, therefore, in these 7 cases x-ray treatment was a failure. Those treated with the 400,000 kilovolt apparatus appeared to be no better off than those treated with the 200,000 kilovolt machine.

The details of the treatment and the dosages used varied from case to case but consisted in every instance in the use of platinum needles or gold seeds implanted into the tumor or around its periphery. Of the 12 patients treated, platinum needles were used in 7, gold seeds in 5. In 2 of the patients in whom platinum needles were used, seeds were implanted as well. The results on the whole were disappointing. In many of the cases the growth was not large. In 7 of the cases the growth was small and confined at first to the anus itself. In only 3 was it obviously large and in only 1 of these was it invading adjacent structures. In 2 there was no record. The histological grade of these tumors was grade 1—1 case, grade 2—6 cases, grade 3—4 cases, no grading—1 case.

If these tumors, as some believe, may be expected to respond favorably to irradiation treatment, the fact that so many of this group were small and not yet invading the surrounding structures should have assisted in obtaining good results. But on the contrary, the results were poor. There was only 1 cure. This patient is alive and well at the end of 11 years after interstitial radiation with platinum needles. Her growth was a small one. The lesion healed slowly, however, and there was a severe local reaction with much pain and tenesmus lasting several months.

In 6 patients in this group there was reasonably good palliation. In these 6 patients there was a temporary complete disappearance of the growth for from 2 months to 4 years. Two of these patients may have been cured of their anal carcinoma, but the end-result could not be known because both died of some other disease. One died 4 years later of a carcinoma of the breast. The other died after 2 years of gangrene of the foot. In both cases the growth was small and both were treated with gold seeds alone.

In 5 cases there was no regression. In all of these the pain and tenesmus induced by the radium treatment in addition to the discomfort already present made them most uncomfortable.

Of the 11 patients who received radium treatment and were not cured, all are now dead (2 of intercurrent disease as stated). The survival period in this group varied from 3 months to 5 years. These results are most disappointing.

COMPARISON BETWEEN THE RESULTS OF THE TWO PRINCIPAL METHODS OF TREATMENT CARRIED OUT

Although there were relatively more small and locally favorable tumors in the irradiation treated group than in the surgical group, the results both as to cure and good palliation were notably superior in the latter. Radical surgery produced cures in 12 of 48 cases (25 per cent) whereas in the irradiated group only 1 in 19 was cured (5.2 per cent). In the majority of the surgically cured patients the growth was large and invasive. In the 1 radium cure case the tumor was small and not invasive. Leaving aside the question of cure, the degree and duration of relief from local symptoms is important. Here again the results of radical surgery are better. In 21 surgically treated cases there was no local recurrence. Thus 41.6 per cent of the patients operated upon experienced complete relief from the local discom-

fort produced by the growth. In only 6 of the irradiation treated cases was there even temporary disappearance of the growth and relief from pain. In 1 of these there was a cure. Two died of other causes, but in 3 there was a recurrence of the disease. There was, therefore, if we exclude the recurrent cases, a degree of palliation in the irradiation treated cases comparable to that obtained by surgery in only 15.8 per cent of the group.

One must conclude, therefore, that irradiation treatment is not as satisfactory as radical surgical excision either as a method of cure or as an attempt to secure relief from the distressing local symptoms of epidermoid carcinoma of the anus and rectum.

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MANAGEMENT OF JAW FRACTURES

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THE treatment of jaw fractures and associated facial injuries, together with severe burns and miscellaneous problems of plastic surgery arising in the Canadian Army Overseas in the late war, was centralized in the plastic surgery division of Basingstoke Neurological and Plastic Surgery Hospital, Royal Canadian Army Medical Corps. This plastic surgery service was organized and commanded originally by Lieutenant Colonel Stuart D. Gordon. The association of neurosurgery and plastic surgery in one hospital was very valuable because craniocerebral injuries so often were associated with wounds of the face and jaws, and in numerous cases the plastic surgeon was able to provide full thickness coverage in loss of skull and overlying scalp after debridement by the neurosurgeon.[1]

In all, around 3,000 patients were treated by the plastic surgery service, or between 5 and 6 per cent of Canadian casualties.[2] Of this number, as might be expected, by far the majority followed the evacuation of wounded from Italy in the late months of 1943 up to "D" Day and with marked increase after that, the work being maintained at a high volume until "VE" Day.

Our experience was varied: In the early period it was concerned with training accidents, with wounds essentially of civilian character, and casualties the result of enemy bombing of civilians. To these were added definitive surgery in late cases of patients arriving from Italy; these patients were treated as long as possible before repatriation. Following "D" Day, until hospitals were established on the Continent there was a period when patients came to us relatively untreated, though with surprisingly little delay. Subsequently, most of the patients with facial injuries received their primary treatment at the hands of one or other of two British maxillofacial surgical units under the command, respectively, of Major Hynes, and Major Fitzgibbon, to whose excellent work we are indebted.

As mentioned previously, our experience covered all phases in the treatment of the jaw wound, whether they resulted from simple trauma or from missile injury. Statistics quoted represent individual patients, not individual fractures of either mandible or maxilla. Of the whole series, detailed analysis has been made of all those patients admitted between January 1, 1944 and July 15, 1945, with the exception of those who died or those who required bone grafts. The figures shown in the tables suffice to exemplify typical features of treatment and complications.

TABLE I.—PATIENTS WITH JAW WOUNDS
JANUARY 1944 TO JULY 1945

	No. cases
Mandibular fractures—All types	369
Maxillary fractures	236
Mandibular fractures—gunshot wounds	256
Mandibular fractures—simple trauma	113

MANDIBULAR FRACTURES

Simple trauma. For purposes of treatment, the jaw is arbitrarily considered in four parts: condyle, or ascending ramus, including the neck; the angle coronoid compound, from base of condyle to the last molar tooth; the ramus or horizontal ramus; and the symphysis.

If reduction is accurate and fixation adequate, these fractures heal well and are united in 6 weeks. Union is estimated by clinical criteria—no "spring" or pain at the fracture site on manipulation or mastication long before it can be confirmed radiologically. If infection occurs, union is delayed for an average of 12 weeks. It is in this type of fracture that nonunion most often occurs. Fractures of the

[1]There were 18 cases of this type.
[2]Based on report of Canadian casualties dated December 28, 1945.

ramus and symphysis are always compound into the mouth, and reduction and fixation are urgent if infection is to be avoided. In our analysis, a delay of 4 days between fracture and reduction, gave marked increase in infection. Surprisingly, a firm tooth in the fracture line appeared to have little influence on the incidence of infection, in fact the evidence pointed the opposite way, possibly because an alveolar gap may have been created in an effort to remove the tooth. Certainly if it represented a single tooth in the posterior fragment, its utility in maintaining reduction was such that it was retained if at all possible. It may be that in older patients in civilian practice, showing a less ideal mouth hygiene than existed among our soldiers, a tooth in the fracture line would be less well tolerated, with less danger of carrying away alveolus in its removal.[1]

TABLE II.—METHODS OF FIXATION OF MANDIBULAR FRACTURES

	No. cases
Interdental and intermaxillary wiring	214
Cast cap splints	88
Interosseous wiring	40
External pin fixation	17
Circumferential wiring	1
External angle wire to plaster of Paris head cap or to bar on cast cap splint	14

Fixation. In methods of fixation our practice differed widely from that of our British confreres who treated the majority of patients with cast cap splints. Perhaps their predilection for splints is due to the loss of teeth and irregular spacing of remaining teeth so frequently found in their patients, even in the age group encountered in the Army. We used cast cap splints in the same relatively edentulous type of patient, but in our soldiers the loss of teeth almost always coincided with their injury. One cannot speak too highly of the fine state of mouth hygiene preserved by the Canadian Dental Corps in the units of our Army.

We of the plastic surgery service were especially fortunate in the caliber of the officers attached to us by the Canadian Dental Corps, in the early days of the unit Major (later Lt. Col.) G. Franklin and, later, Lieutenant Colonel V. Jekill, Major A. T. Roger, M. B. E., and Major G. MacDonald, M.B.E. The latter two were most intimately concerned with the work in the operating room and the wards. Each patient was seen by surgeon and dental officer in consultation and the method of treatment determined. In many cases, this was carried out by the dental officer until fixation was removed and the patient was again seen in consultation for final appraisal before discharge. In all cases, the dental officers assisted in the routine postoperative care in the wards. Patients, with complications from the beginning or in whom complications developed, were operated on by the surgeon with the assistance of dentist to provide fixation. In this way, our usual aggregation of 50 or 60 patients with fractured jaws was under the closest observation with a minimum of overlapping. Fracture of the mandible of civilian type due to simple trauma is usually of ramus (including symphysis) or angle coronoid, and the opposite condyle. A condyle fracture alone, even in the presence of luxation of the head is treated by fixation in good occlusion for 2 weeks to prevent shortening on the side of fracture. Early mobilization is necessary to avoid trismus which is prone to occur in such case after prolonged fixation of the jaws.

Angle coronoid fracture is not likely to be compound but the posterior fragment is prone to upward and inward displacement with consequent malocclusion. Reduction may be retained by a bite block and intermaxillary fixation but is usually disappointing, both in reduction and fixation. Open reduction and interosseous wiring is most satisfactory, combined with interdental and intermaxillary (I.D. and I.M.) wires. Pins may be used in this type of fracture if preferred. Angle coronoid fractures unite freely, but upward displacement of the posterior fragment must be guarded against, for, if present, it seriously interferes with fitting of a denture and, sometimes, with occlusion and mastication.

Ramus fractures are always compound into the mouth. Treatment is urgent on this account, though not an emergency, unless through bilateral ramus fracture the patient is unable to swallow. In such case it is im-

[1]From an analysis of 233 cases of fracture due to simple trauma in this series 1940 to May, 1944.

portant that he be treated face downward until the jaw is fixed to prevent him drowning by aspiration of blood and saliva. As previously pointed out, a tooth in the fracture line should be retained if it is alone or is one of two in the posterior fragment and is firm. If the ramus is edentulous or the posterior fragment is edentulous the fracture must be treated in the same way as an angle fracture. In most cases of ramus fracture, eyelet wires and intermaxillary wires, or some suitable combination of arch wire, or arch bar, and intermaxillary wires give satisfactory reduction and fixation. The fracture is tested for union in 5 to 6 weeks, and should not be considered a case of nonunion for at least 3 months unless gross infection has occurred.

Nonunion of ramus and symphysis fractures may be due to failure of reduction and fixation, but occasionally it is difficult to explain. The chief factor in nonunion is infection. Nonunion is to be expected in case of bone loss involving the whole depth of the mandible. It is not important in the condyle except in consideration of adjacent soft tissue damage leading to trismus. Movement must be started early in from 2 to 3 weeks, to avoid such an occurrence. Due to whatever cause, nonunion is treated along the lines adopted for fracture due to gunshot wounds with loss of bone, though, of course, the reconstruction is far less formidable.

TABLE III.—GUNSHOT WOUNDS OF MANDIBLE

	No. cases
Gunshot wounds with ramus fracture	154
Gunshot wounds with condyle fracture	37
Gunshot wounds with angle coronoid fracture	65
Mandibular fracture with bone loss	72
Mandibular fracture with soft tissue loss	20

Gunshot wounds of mandible. "Bone loss" is a term used in this group to indicate loss of a section or sections, the full depth of the jaw, and thus to distinguish the case as a problem in treatment different from the fracture due to simple trauma. Where a portion of the alveolus is knocked off in association with a fracture through the body of the bone, simple débridement of bone and soft tissue wound with closure of the latter to cover the bone and with the type of fixation used for a fracture due to simple trauma is the treatment. A free graft to deepen the sulcus is commonly necessary before a dental prosthesis can be fitted. Similarly, if a piece of bone is fractured from the lower border of the ramus, it usually retains enough soft tissue attachment to provide a blood supply and may be ignored. The troublesome case is that in which there is gross comminution of bone. A thorough débridement must be done, that is scrupulous removal of all bone fragments with doubtful blood supply, of tooth fragments, and devitalized soft tissue, and complete closure of the soft tissue wound. If there is not enough soft tissue available inside the mouth for restoration, mucosa must be sewed to skin edge over the bone ends. It is quite easy to locate and remove bone fragments detached from soft tissue in the recent wound, but if they are allowed to remain, the wound will suppurate and in the presence of the resultant edema, granulation, and scar tissue, it may be impossible to locate them.

Fixation of the fracture with bone loss is best done with sectional cast cap splints if teeth are available. Impressions are made for these at the time of débridement and they are cemented in place 1 or 2 days later, an anesthetic being unnecessary. This splint retains the normal relative position of the fragments and is the final fixation until union occurs after bone graft. In case there are not enough teeth available, the alternative fixation is by external pins.

Fractures with any appreciable amount of bone loss require a bone graft for union if deformity is to be avoided. In case of nonunion of a fracture due to simple trauma, or if bone loss is less than ½ inch, the graft may be of medullary chips. The ends of the fracture fragments must be freshened and intervening scar tissue removed. Enough of the outer cortex adjacent to the fracture must be removed to get free contact between the chips and their host. The wound is not drained and a pressure bandage is applied for 48 hours to prevent any possibility of hematoma.

Bone grafts in mandibular fractures. In larger defects, a combination of cortical bone and medullary chips is used. The graft is obtained from either iliac crest which is exposed and split longitudinally for a little more than

TABLE IV.—BONE GRAFTS IN MANDIBULAR FRACTURES

	No. cases
Gunshot wound bone defects; iliac cortical block and medullary chips	70
Simple trauma; cancellous graft	32
Total series 1940–1945	102

the estimated required length of graft. The inner half is removed for a depth of about ⅔ inch by checking with an osteotome, then, with a narrow osteotome, a considerable yield of medullary fragments may be obtained. If only medullary bone is required, the cortical block is driven back into its place. If the cortical block is to be used as graft, a moderate amount of medullary bone is left attached to it. The jaw fragments are now exposed and prepared as described previously, the cortical block is suitably shaped and wired firmly to the fracture fragment at each end, cortical side out, and small medullary chips are packed around its ends and beneath it.

Penicillin and chemotherapy have markedly cut down the morbidity in these cases. Bone grafting can usually be done 3 to 4 weeks after the primary débridement and closure of soft tissues instead of in as many months. Practically all bone grafts were done in England as a routine measure, in spite of pressure of other work, in view of the fact that the jaws had to be fixed in occlusion until union was procured, and of possible delays in repatriation and in resumption of active treatment at home. In this way it was possible to avoid much discomfort and inconvenience to the patient. Actually, firm clinical union was the rule in 6 weeks from operation and the majority of these patients were observed to this point. It is probably unwise to send a patient on a stormy Atlantic crossing with his jaws wired together.

Complications of bone graft were few: There was no case of osteomyelitis of ilium. An abscess occurred in the soft tissues outside the jaw in 5 cases, but in each case yielded to simple drainage and chemotherapy without loss of graft. We saw only 1 case of nonunion after bone grafting, and 1 other case in a repatriated patient is known to us. A complete survey of these repatriated patients has been impossible to date.

TABLE V.—FRACTURES OF THE MAXILLA

	No. cases
Total maxillary fractures[1]	236
Maxillary sinus "clean-out" Caldwell-Luc	75
Maxillary sinus "blow-out"	19
Nonunion of mid third fracture[2]	1

[1]Series of cases January, 1944 to July, 1945.
[2]Union secured with bone graft.

Trismus is rarely troublesome in mandibular fractures but is a feature in fractures and gunshot wounds of the condyle and coronoid. It is most common in what appear to be relatively simple through and through wounds of the middle of the face from bullets. Probably the mechanism is the same in both cases and is due to side to side adhesion of muscle and fascial planes. It can be avoided by early mobilization but, once established, is very difficult to overcome. Forced mobilization under anesthesia only results in recurrence in aggravated form; dental exercisers are disappointing; the best results are from graduated bite blocks worn 24 hours daily until the opening is enough to admit solid food.

MAXILLARY FRACTURES

Fractures due to simple trauma range from fracture of a portion of the alveolus to complete separation of the maxilla from the skull, the mid third fracture or floating maxilla so often seen in motor cycle accidents and frequently complicated by being comminuted through palate and alveolus. The alveolar fracture is easily treated by wiring the teeth in occlusion. The more severe type requires repair of the mucoperiosteum of the palate, if this bone is broken, and in addition to interdental and intermaxillary wires, a plaster of Paris chin cradle and head cap connected by two lateral rods adjustable through universal joints. The problem of insufficient remaining teeth is met by wiring a Gunning splint to the alveolus. The simple alveolar fracture unites in 3 weeks; the more severe fracture requires fixation for 4 to 6 weeks. Infection and nonunion are rare.

When a missile traverses through the cheek and maxillary sinus and lodges, perhaps, in the pterygoid fossa or the neck on the opposite side, it is usually quite easy to remove it by following the track or by making a counter-incision in the neck. We felt that removal was

wise for fear of infection from the sinus and danger of secondary hemorrhage from the large vessels of the neck. Many bone fragments were driven into the maxillary sinus, and débridement and closure of the wound were combined with a Caldwell-Luc antrostomy when the antrum could be cleaned out and indirect drainage of the wound track provided by making a large window into the nose.

In cases in which the missile traversed the face and which we termed a "blow-out" because of the wide destruction of soft tissue of the cheek at the site of exit, careful débridement of the wound was done, free drainage into the nose provided from both maxillary sinuses though this was usually present from the nature of the wound, and every effort made to close the cheek wound by undermining or by rotating a cheek flap. No attention was paid to lining in such case in the hope that it would regenerate from the antral mucosa, and this appeared to be the case. Careful débridement of bone and devitalized soft tissue and avoidance of dead space are essential. In some cases, especially if a good deal of the zygoma was lost, dead space was obliterated by rotating a flap of temporal muscle. Penicillin and chemotherapy undoubtedly are of great assistance to the natural defensive forces against infection, but are of no avail unless débridement is scrupulous and fluid collection is avoided. Hemorrhage, often severe in this location, is usually controllable with fibrin foam but in a few cases it was necessary to ligate the external carotid artery.

TABLE VI.—COMPLICATIONS OF FACIAL WOUNDS

Secondary hemorrhage	6
Osteomyelitis	15
Tracheal obstruction (tracheotomy)	34
Gastrostomy required	1
Eye enucleation or evisceration	66
Eye trauma	80

COMPLICATIONS IN FACIAL WOUNDS

The relative rarity of secondary hemorrhage is remarkable. Intramuscular penicillin was started with the first treatment of our casualties and was continued in regular dosage throughout evacuation to base hospital. In no case did we find spreading infection on arrival, and to penicillin treatment and to careful débridement must be attributed the rarity of secondary hemorrhage. Tracheotomy was wisely done by the maxillofacial surgical unit in all cases in which there was any doubt of airway obstruction during evacuation. It was only occasionally required otherwise.

Operation in these cases is not an emergency measure unless because of hemorrhage, respiratory obstruction, or inability to swallow. In fact it should be deferred for a few hours, for on arrival the patient is tired, cold, and hungry. Clinical check is followed by immediate x-ray examination in those cases in which high priority for operation is indicated. Removal of dirty, blood-caked clothing, a hot bath, hot nourishing fluids, and a sedative lead to a few hours of sleep and relief of "battle fatigue," and make the patient a much better operative risk. In case clinical examination of the chest, checked by radiological examination if necessary, shows evidence of aspirated fluids, these are removed through a bronchoscope before operation.

Credit to Major R. A. Gordon, our anesthetist, and his staff cannot be too high. Preoperative resuscitation was under his supervision, and he was continually alert for postoperative pulmonary complications. He frequently had occasion to aspirate large amounts of blood and mucus saliva from the lungs before operation, and in this way and in prompt bronchoscopic cure of collapse of the lung when it occurred after operation, chest complications were avoided. Blood transfusion was done freely during operation, for it was found more economical to keep the patient out of shock than to resuscitate him when shock had already taken place. These operations were frequently prolonged and often attended with a good deal of unavoidable hemorrhage.

There was only 1 death in our cases of jaw and facial wounds:

Private L. S., G41607. Shell wound enemy action. Wounds consisted of compound fracture of right humerus, both jaws, and chest received July 28, 1944. Treatment No. 5 maxillofacial surgical unit, débridement of arm and plaster cast, débridement of jaw and face and intermaxillary fixation were carried out. He was admitted to Basingstoki Neurological and Plastic Surgery Hospital August 5, 1944. Patient was

very ill but as x-ray examination showed multiple bone and tooth fragments in the fractures of both jaws, and the previously sutured facial wounds were partially separated exposing bone, operation was carried out. Two bottles of blood were given during operation. Operation consisted of débridement of tooth and bone fragments from both jaws, interosseous wire to lower jaw, débridement of soft tissues, and repair to cover exposed bone. His condition was not good enough to permit taking care of the arm fracture. Penicillin was given in 100,000 units daily; sulfathiazole grams one every 4 hours for 5 doses; intravenous glucose saline 5 per cent, 3,000 cubic centimeters daily. Condition was improved until August 9 when he became confused mentally and lethargic. He vomited occasionally. Urinalysis was 2 plus albumen, red blood cells and white blood cells, nonprotein nitrogen 436. Steady deterioration and uremia occurred resulting in death on August 16, 1944, nonprotein nitrogen 450.

This man had had 12 transfusions before he was admitted to our care. Necropsy showed his kidney tubules plugged with blood. It was a remarkable feat that our soldiers were supplied with blood so freely. Even at our level, only Type O blood was supplied. Transfusion accidents were very rare, and in our experience this was the only case in which there was a fatality.

FEEDING ROUTINE FOR JAW CASES

Types of diets. (a) Jaw fluids. (b) Jaw No. 1. (c) Jaw No. 2.

Methods of feeding. Patients with gunshot wounds of mouth are fed a completely fluid diet of 1800 calories, plus a special tube feeding of 800 calories. Patients should be fed in a prone position in order to prevent regurgitation of the liquids. The patients are fed with a rubber tube on the end of a large glass syringe or a bulb syringe.

Jaw fluid diet consists of 1800 calories. If patient is able to purse the lips and does not have a paralyzed tongue, he may drink the fluids from a feeder. Otherwise patient has rubber tube inserted between the molars and the cheek and the liquid is poured slowly through the tube from a feeder. If opening is inadequate, fluids may be forced gently between the teeth by a bulb syringe.

Jaw 1 diet consists of 2600 calories. All the food is puréed, and all beverages strained. This diet is fed to the patient all the time the splints are on. Patient carries the puréed food to the lower lip by spoon, and then sucking and pushing (by the finger) gets the food into the mouth.

Jaw 2 consists of 2600 calories. Only the meat remains puréed; no raw salads are given. This diet is given when the patient has had the splints removed.

To all diets is added ascorbic acid, 100 milligrams, and vitamin D oil, ½ ounce daily.

The patient must be encouraged to eat the jaw 1 diet at the earliest possible moment. This jaw 1 diet is better balanced, has more calories, and gives greater variety than the fluid diet. The jaw fluid diet is used only for 24 to 48 hours, except in the case of patients with gunshot wounds and special patients who may need fluid diet for a longer time because of particular injury.

It is always important that the food be presented to the patients in as attractive a manner as possible and that a wide variety of tastes to attract his palate be used.

SUMMARY

An analysis of fractures of lower and upper jaws is submitted. These fractures were of two types, namely, civilian type and those due to gunshot wounds. Types of fixation are indicated in their respective frequency of employment.

With careful débridement associated with penicillin and chemotherapy and by carefully planned closure of soft tissue wounds, it was possible to avoid much soft tissue deformity. Similarly, in comminuted fracture of the mandible, treatment consisted of careful débridement of all planes of the wound especially aimed at removal of any bone fragment without soft tissue attachment or with doubtful blood supply, obliteration of dead space, and complete closure of the overlying soft tissue without drainage. Following this procedure, there was rarely any further sign of infection necessitating further débridement. Bone grafting was done within a month after primary closure in those cases in which it was indicated, and was practically always successful with minimal complications.

Secondary hemorrhage was rare, probably due to adequate surgery and avoidance of infection. Penicillin and chemotherapy are of great value in limiting infection, but the greatest factor is still careful surgery.

In civilian type fractures with nonunion or in fractures with a gap of less than ½ inch, bone graft was of medullary chips alone from the iliac crest. In larger gaps, a block of cortical and medullary bone was wired firmly to both fragments of mandible, supplemented by medullary chips beneath it and around the ends.

Some practical suggestions regarding the care of wounds of this kind and regarding dietary requirements are included.

SURGERY OF THE POSTERIOR INTEROSSEOUS BRANCH OF THE RADIAL NERVE

Analysis of 58 Cases

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FRANK H. MAYFIELD, Lieutenant Colonel, M.C., Cincinnati, Ohio

LESIONS of the posterior interosseous branch of the radial nerve have been considered unamenable to surgical repair by many surgeons. Reluctance to attempt repair has been based on the belief, first, that gaps could not be overcome because of the straight course of the nerve; second, that widespread arborization prevented end-to-end suture; and third, that tendon transplantation provides an adequate substitution with a much shorter convalescence. Experience in the Neurosurgical Section at Percy Jones Hospital Center indicates that these objections are not valid.

The primary purpose of this paper is to present the data from 58 patients treated surgically. These data demonstrate that surgical repair may be accomplished satisfactorily in a high percentage of cases and that the results justify the attempt. It is our further purpose to discuss in some detail the diagnosis and surgical treatment employed.

ANATOMY

The radial nerve, after giving off motor branches to the extensor carpi longus and brachioradialis, divides just distal to the elbow into its two terminal branches, the superficial radial nerve and the deep or posterior interosseous branch. The latter nerve then passes deep to the extensor carpi longus and enters the fibers of the supinator muscle. Coursing obliquely around the head of the radius it emerges from the supinator fibers on the posterior aspect of the upper one-third of the forearm. Textbooks of anatomy depict immediate branching of the nerve as it leaves the supinator fibers. In our experience it often arborizes 1 or more inches below the supinator muscle.

Read before Surgical Conference, Sixth Service Command, July 28, 1945, Chicago, Illinois.

The nerve supplies the extensor communis digitorum, extensor carpi ulnaris, extensor pollicis longus and brevis, and abductor pollicis longus. No significant sensory component is present in the nerve.

DIAGNOSIS

Paralysis of the muscles which this nerve supplied produces a characteristic deformity of the hand (Fig. 1). Dorsiflexion of the wrist is preserved by the extensor carpi longus. Paralysis of the extensor communis digitorum renders extension of the proximal phalanges of the fingers impossible. Extension of the distal phalanges is preserved, since this movement is performed by the interossei and lumbricales. Paralysis of the extensors of the thumb prevents active extension of all joints of the thumb and paralysis of the long abductor prevents abduction of the thumb in the plane of the palm. The thumb in repose assumes a position of slight flexion being immediately ventral to the index finger. When forceful extension of all digits is attempted, apparent extension of the index finger may be accomplished in a passive manner by strong contraction of the adductor and the opponens pollicis.

SURGICAL TECHNIQUE

Exposure of the deep branch of the radial nerve is secured through an incision (Fig. 2) overlying the fascial plane between the brachioradialis and biceps muscle on the lateral aspect of the distal portion of the upper arm, extending lateral to the antecubital fossa and over the posterior aspect of the upper portion of the forearm between the brachioradialis and the extensor carpi radialis. The radial nerve is identified between the brachioradialis and the biceps tendon and dissected downward to the site of injury. Care must be taken to preserve

Fig. 1. Typical deformity on attempted extension of all digits in paralysis of posterior interosseous nerve.

the motor branches to the brachioradialis and extensor carpi longus. The nerve is then picked up immediately below the supinator fibers by separating the extensor carpi longus and extensor communis digitorum. The proximal neuroma and distal glioma are resected back to healthy fascicules. Gaps measuring up to 5.0 centimeters are easily overcome by freeing the nerve up to its parent trunk and flexing the elbow to 90 degrees. Anastomosis is accomplished with sutures of .003 tantalum or No. 000000 black silk placed through the epineurium of the divided nerve ends. No stay suture has been employed except in cases in which tension on the suture line was thought to be unduly great. Tantalum foil

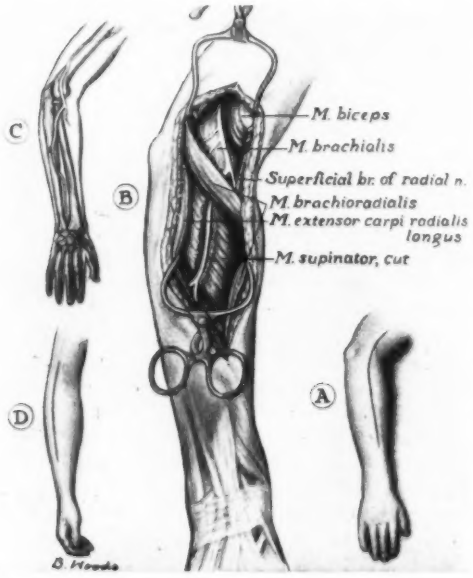

Fig. 2. Surgical exposure. A, Line of incision—forearm prone, elbow flexed; D, line of incision—elbow straight; C, diagram of course of nerve with arm in position A; B, incision open—nerve exposed.

Fig. 3. Full recovery of all muscles 10 months after operation.

has not been used. The elbow is immobilized in the flexed position by means of circular plaster with the forearm in slight pronation, the wrist in cock-up, and the fingers and thumb free. The plaster is removed in 4 to 5 weeks and immediate physiotherapy is begun without restriction upon the rapidity with which complete extension of the elbow is secured.

RESULTS

Of the 58 patients (Table I) subjected to surgical exploration of the deep branch of the radial nerve, neurorrhaphy was done in 39; in 2 cases it was necessary to repair the divided nerve by means of an autogenous graft obtained from the superficial radial nerve; the nerves in 14 cases required neurolysis only. In 3 cases, for reasons which will be described, it was impossible to secure repair of the nerve.

For appraisal of results the patients have been divided into two groups; group I, includes cases in which repair was performed prior to May 1945; group II, those cases in which repair has been carried out since that time. Though 2 of our patients have shown earliest signs of recovery during the seventh and eighth months, we have included for final evaluation all cases in which repair was effected 6 months or more prior to this report. Of the 37 cases comprising group I, neurolysis only was performed in 9, end-to-end suture in 24, the use of an autogenous graft to overcome

TABLE I.—SURGICAL EXPLORATION OF POSTERIOR INTEROSSEOUS NERVE, OCTOBER 1943 TO OCTOBER 1945

Type of repair	Group I 6 mos. or more postoperative	Group II Less than 6 mos. postoperative	Total cases
Neurorrhaphy	24	15	39
Repair with graft	2	0	2
Neurolysis	9	5	14
Irreparable	2	1	3

Fig. 4. Partial recovery demonstrating residual paralysis of extensor and long abductor of thumb 6½ months after operation.

gap in the nerve in 2, and complete failure to secure repair in 2 cases.

The deep branch of the radial nerve, being purely motor, lends itself to simple evaluation. We have divided our patients into those who have obtained what we call full recovery (Fig. 3), in whom all the muscle groups supplied by the deep branch of the radial nerve function with at least 50 per cent of normal motor power; partial recovery (Fig. 4), in whom recovery in some, but not all, of the muscle groups supplied by the nerve has taken place, or in whom all muscle groups have recovered, but one or more of them in a defective manner (Fig. 5).

Evaluating the cases of neurorrhaphy observed longer than 6 months after operation (Table II), in the 26 patients so treated full recovery has been obtained in 19 or 72 per cent of the cases. Partial recovery has been noted in 3 cases, and failure of any evidence of muscle return in 4 cases. Two of the patients with partial recovery were operated upon less than 8 months ago and further evidence of recovery in the muscles still paralyzed is anticipated. It should be noted that the 26 cases considered for evaluation of end-result includes the 2 patients in whom graft was necessary to secure repair.

DISCUSSION

The data leave little doubt about the feasibility of repairing this nerve in a high percentage of cases. Attempt to repair the divided nerve met with failure in 3 cases, representing 6 per cent of the total group. One of these patients had been struck by fragments of a phosphorous shell and had, in addition to the soft tissue damage caused by the metal fragments, extensive phosphorous burns of the proximal third of the forearm. The area normally occupied by the deep branch of the radial nerve was replaced by such dense scar tissue that identification of the nerve was impossible. The remaining 2 cases of failure were in patients with extensive soft tissue damage and severe comminuted fractures of the upper end of the radius with generous callus formation. In these cases, as in the first, scar tissue and callus replaced the area through which the deep radial nerve coursed.

Fig. 5. Partial recovery demonstrating residual partial paralysis of extensor communis digitorum 7 months after operation.

The 4 patients in whom repair was secured, but in whom recovery has not taken place, deserve special consideration. In 1 of these patients, E. S., the original injury to the nerve was incurred 3 years prior to surgical exploration, and was the result of a surgical accident during operative removal of the head of the radius in civilian life. Because of the long period of time which had elapsed prior to repair of the nerve, only 4 months postoperative observation was allowed before tendon transplantation was undertaken, for at that time electrical reactions indicated complete denervation. In the second patient, A. M., end-to-end anas-

TABLE II.—RESULTS FOLLOWING NEURORRHAPHY OBSERVED 6 MONTHS OR MORE POSTOPERATIVELY—TOTAL CASES 26

Degree of recovery	No. of cases	Per cent of cases
Full recovery	19	72
Partial recovery	3	12
Failure	4	16

tomosis was performed, but with considerable tension present on the suture line. This man failed to recover and at reoperation, 3 months ago, the suture line was found to have separated, and reanastomosis was carried out. A third patient had a 9 centimeter gap in the nerve following resection of the neuroma and glioma and anastomosis was accomplished only with considerable difficulty and with gross interstitial fibrosis still present in the distal segment of the nerve. This man has not recovered 7 months following the procedure and it is felt that the prognosis for recovery is not good. In the fourth patient a 3½ centimeter autogenous graft was employed to repair the nerve. Tendon transplantation has been performed in this man 5 months after operation because of the poor prognosis which we considered the graft to entail.

Of the 2 cases in which autogenous grafts were employed, one has shown full recovery beginning 8 months following operation, a 2.0 centimeter autogenous graft having been employed.

In the cases of recovery the only residual disability has been slight motor weakness, and the condition probably will approach normal with time and use. There can be no doubt that function following repair of the nerve is superior to the results ordinarily achieved with tendon transplantation.

The frequent and complete recovery following neurorrhaphy of the deep branch of the radial nerve appears to exceed that obtained with other nerves. This perhaps is explained by the fact that it is a pure motor nerve and because the muscles it supplies perform comparatively crude movements. The latter may mask minor defects in motor recovery more obvious in finer movements such as those mediated through the intrinsic muscles of the hand.

SUMMARY AND CONCLUSIONS

The data from 58 operations on patients with paralysis of the posterior interosseous branch of the radial nerve have been presented. These cases have been divided into two groups for analysis, based on time elapsed since operation. In 26 cases more than 6 months have elapsed since operation, in 15 cases less than 6 months.

Of the 58 cases in which exploration was carried out, end-to-end suture was accomplished in 39, in 2 autogenous grafts were required, neurolysis was done in 14, and repair was impossible in 3.

Twenty-six patients with end-to-end suture have been followed more than 6 months. Nineteen, or 72 per cent, of them show complete recovery, 3 partial recovery, and 4 failure.

These results warrant the conclusion that repair can be done in most cases and that tendon transplantation is not justified as a primary procedure.

HISTOPATHOLOGY OF THE GASTRIC SEMISQUAMOUS EPITHELIAL LAYER

FREDERIC DURAN-JORDA, M.D. (Barcelona), Manchester, England

HAVING described previously (1, 2), the semisquamous epithelial layer (Fig. 1) which covers the normal gastric and intestinal mucosae, we are now going to describe the different histopathological syndromes found by making a study of a fair number of resected specimens of stomach.

PATHOLOGY OF THE GASTRIC SEMISQUAMOUS EPITHELIAL LAYER

The specimens were carefully studied for the presence of all abnormalities, principally erosions, and afterward we took a photographic record of the fresh specimen, or made a schematic drawing, so that after formalin vapor fixation we could select the parts which appeared to be pathological in the fresh specimens. We adopted this procedure because after fixation the mucosa assumes a dark brownish color, and small alterations and erosions fade out and are very difficult to find.

Erosions. We studied the erosions very carefully as we hoped to gain a better understanding of the problems of ulceration through these small, gastric lesions. In the first place, we supposed that any erosion indicated a preulcerative process, or was actually a very tiny ulcer, and we were extremely careful to avoid the neglect of any details. We selected the whole portion containing the erosion for study and made it into a paraffin block for serial section. As a result of this, we have been able to describe the full meaning of erosions, that is, the erosions which represent preulcerative processes, and the erosions which represent the postulcerative processes, and which will be described later.

Preulcerative erosions. Our observations made during the study of the preulcerative lesions disagree completely with the descriptions of the same process as given by different authors, as they have not been able to consider the significance of the semisquamous epithelial layer when making a study of these lesions.

Our investigations of the preulcerative lesions have brought us to the conclusion that they have two typical characteristics: One is the lesion of the semisquamous layer itself, and the other is in the mucous membrane.

The lesion in the semisquamous layer itself is represented by an extensive infiltration of round cells and polymorphs which are linked by means of a cellular bridge with the submucosa, in a similar way to that which takes place in ulcerative colitis. This bridge contains occasionally, small capillaries, and the layer may be thick and irregular in appearance (Fig. 2).

The lesion in the mucous membrane is characterized by an intense disorganization of these glands and some of them appear to be breaking up their morphological structure, and there is an extensive infiltration of polymorphonuclear and round cells. It is still possible, however, to recognize normal parts of the gastric mucosa (Fig. 3).

Ulcer. The study of ulcers was made by means of a similar technique to that used for investigation of the erosions, and the whole ulcer was embedded in a paraffin block and made into sections. We carried out our observations on serial sections, and these were of great interest, principally in the edges of the ulcer at the union between the normal gastric mucosa and the ulcer itself.

As we had expected, we found that the semisquamous epithelial layer was missing from the gastric ulcers, and by making sections of the whole ulcer, it could be appreciated that the layer disappeared after covering the normal mucous membrane at the edges of the ulcer, and was absent from the center of the ulcer (Fig. 4). In some ulcers, it could be seen how the crater contained some slough

From the Department of Pathology, Ancoats Hospital, Manchester, England.

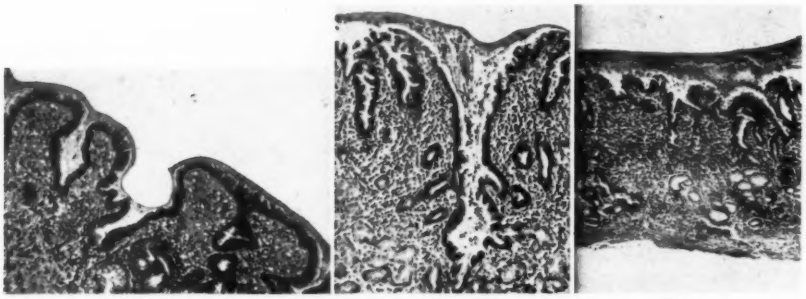

Fig. 1. Fig. 2. Fig. 3.

Fig. 4.

Fig. 1. After formalin vapor fixation. The semisquamous epithelial layer showing a unicellular structure in some places.

Fig. 2. Preulcerative process. Notice the bridge joining the semisquamous epithelial layer with the submucosa and also the cellular infiltration.

Fig. 3. Further advancement of the preulcerative process. Observe how the semisquamous epithelial layer is joined by bridges with the submucosa. Notice also the disorganization of the mucous membrane.

Fig. 4. A large, simple ulcer of the stomach. Notice how the semisquamous epithelial layer finishes at the edges of the ulcer. It is remarkable that the crater of the ulcer does not show any mucous material.

tissue, and it was doubtful if this really represented the semisquamous epithelial layer, but further observations cleared up this doubt. When the ulcer was stained with thionin it could be seen that the crater was full of microorganisms, some of them included in parts of the tissue itself, forming what appeared to be colonies. When stained with mucin stains, the material contained in the crater of the ulcer had none of the characteristics of mucus. Another observation we made was that in some ulcers there was a foreign body included in the crater of the ulcer. Studying the ulcer crater by high magnification, it can be seen that the semisquamous tissue disappears at the edge as an independent morphological structure, and the crater itself is formed by an accumulation of round cells which are linked together by fibrotic tissue and plasma (Fig. 5).

After these investigations, therefore, we can conclude that the crater of the ulcer is without any protection from the semisquamous epithelial layer.

At the edge of the ulcer and covering the mucous membrane, can be found capillaries or venous dilatations, some of them being the largest vessels we have found in the semisquamous epithelial layer of the gastric mucosa (Fig. 6).

The protective function of the semisquamous epithelial layer is fully demonstrated by the study of the process of cicatrization of the ulcer. We have divided the mechanism of healing and mucous membrane reconstruction into 4 parts.

In the first one we can see how the semisquamous epithelial layer begins to grow from the edges and covers the upper part of the ulcer, and in some cases a bridge is formed, and under the cover of the new layer the mucous membrane spreads toward the center of the ulcer (Fig. 7).

By the second process the mucous membrane cells, using the protection of the bridge formed by semisquamous cells, form islands of mucous cells floating in the space between the protective layer and the new mucous membrane, and these free accumulations of cells will form new glands (Fig. 8).

The third process can be found in the crater of the ulcer itself, where occasionally there are islands of mucous membrane cells which ap-

Fig. 5.

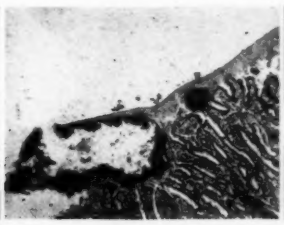

Fig. 6.

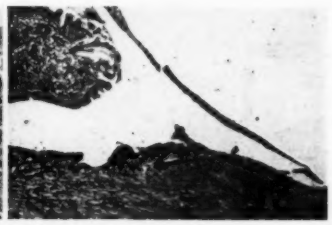

Fig. 7.

Fig. 8.

Fig. 9.

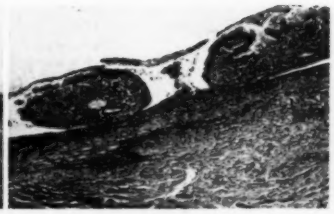

Fig. 10.

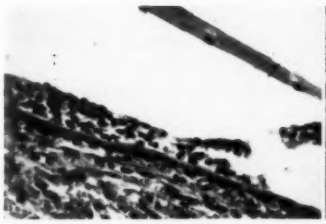

Fig. 11.

Fig. 12.

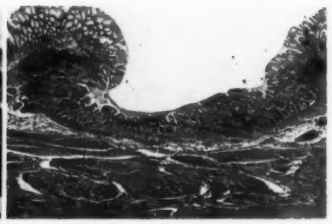

Fig. 13.

Fig. 5. A gastric ulcer, at the edge of which it can be seen how the semisquamous epithelial layer joins with the crater of the ulcer and disappears as a detached body.

Fig. 6. A large blood vessel at the edge of a gastric ulcer.

Fig. 7. The edge of a gastric ulcer. Notice how the monocellular mucous membrane spreads toward the crater and is protected by the semisquamous epithelial layer.

Fig. 8. An island of mucous membrane cells which are growing to form new gastric glands, protected by the semisquamous epithelial layer.

Fig. 9. A patch of glandular tissue in the center of a gastric ulcer from which the mucous membrane spreads toward the edges of the ulcer.

Fig. 10. The mucous membrane throwing out projections which will form new glands. All are protected by the semisquamous epithelial layer.

Fig. 11. Details of the new unicellular mucous membrane layer in which can be seen cells with a cuboid aspect. Notice the thickness of the semisquamous epithelial layer.

Fig. 12. Postulcerative process. Notice the complete mucous membrane which is found to be unicellular in some cases, and the presence of a strong semisquamous epithelial layer.

Fig. 13. Final healing process of an ulcer. Notice what appears to be an atrophic mucous membrane, and a complete semisquamous epithelial layer.

pear to be protected by semisquamous epithelial cells, and under this protection they are able to begin another process of healing by spreading toward the edge of the ulcer (Fig. 9).

The fourth process is more a process of reconstruction than a proper healing mechanism. From the layer of new mucous membrane cells we could see how they project groups of cells like fingers, and these projections go toward the making of new glands. But in this case, the whole mucous membrane is fully protected by a new semisquamous epithelial layer (Fig. 10).

It is important to mention here that when studying the cellular morphology of the new healed mucous membrane, one is struck by the fact that there are present a large quantity of polymorphonuclears, leucocytes, which, by following exactly the same mechanism of growing their protoplasm and loosing their nuclei

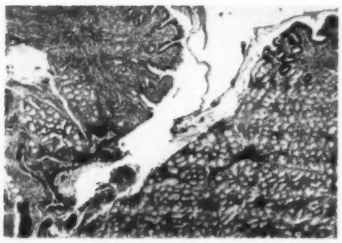

Fig. 14. Pseudoulcer from the pyloric region of a stomach, which shows a gap in the mucous membrane. Notice that the gap is covered by the semisquamous epithelial layer, which comes in contact with the Brunner glands.

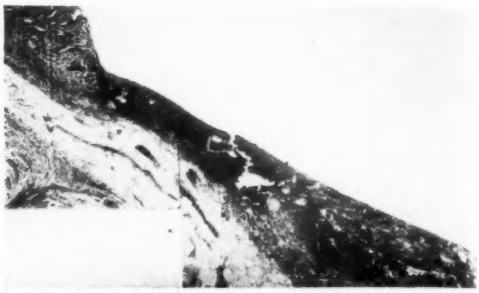

Fig. 15. A gap in the pyloric region which is occupied by what appears to be a venous sinus.

as we have studied in the milk and pus cells (3, 4), settle there and form the new mucous membrane layer. The cells of the new mucosa layer have the appearance of cuboid cells with a nonmucous protoplasm, very similar to some epithelial cells, which form the wall of breast cysts, or the glandular cells making up the structure of the acini in colloid goiter, and later on, these cuboid cells begin their secreting process and have the aspect of normal mucous membrane cells (Fig. 11).

Postulcerative process. Studying the mechanism of ulcer cicatrization, we could recognize the difference between an erosion which precedes a gastric ulcer, or an erosion which follows it. It is necessary again to remark that the picture of a postulcerative process has been taken by a number of authors to mean a preulcerative process. The basic difference is that in the postulcerative lesion there is a perfect and what appears to be healthy semisquamous epithelial layer, with some cellular infiltration present, but it is not linked with any cellular bridges as we have seen in the preulcerative process, and on the other hand, the mucous membrane has the appearance of a very atrophic mucosa with a very good mucous cellular layer. Sometimes this is monocellular and without any other glandular structure, and the appearance of the mucous membrane cells in cuboid form, as we have previously explained in the description of the formation of the new mucous membrane (Figs. 12, 13).

Pseudoulcer. It is interesting to find when studying different gastric mucosa, how, occasionally, in different parts of the stomach, but principally in the pyloric region, it is possible to observe a gap in the mucous membrane where the whole mucous membrane layer is missing, but this part is without any cellular reaction of the submucosa, and the gap is covered and protected by what appears to be a healthy semisquamous epithelial layer.

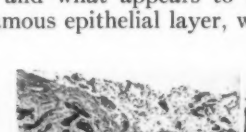

Fig. 16.

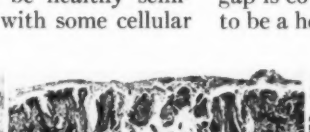

Fig. 17.

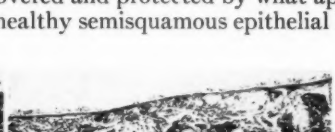

Fig. 18.

Fig. 16. Gastric carcinoma showing ulcerative process.
Fig. 17. Part of a gastric carcinoma surrounded by gastric glands with a normal aspect. Notice the semisquamous epithelial layer covering the whole structure.

Fig. 18. Section of tissue removed from a gastric carcinoma which shows a total disorganization of the gastric glands but what appears to be a well defined semisquamous epithelial layer.

In some cases the spaces where the mucous membrane is missing are occupied by large blood dilatations, similar to small angiomatous conditions (Figs. 14, 15). This is one of the facts which called our attention when we began to study the semisquamous epithelial layer. The absence of the mucous membrane in the pyloric region has been confirmed by studying different stomachs, and it appears that probably in some gastric mucosae, there is an embryonic defect at the point where the two different histological structures meet. This gives place to a gap in the mucous membrane. If the gap is a genuine one, it can be proved by the fact that the whole of it is protected by the presence of a semisquamous epithelial layer. The study of these pseudoulcers convinced us that if histologically, they give a very abnormal picture they may have very little pathological meaning because (a) there is a very good protective layer present and (b) there is an absence of any cellular infiltration of the gastric wall, which disagrees entirely with the pathological picture of inflammation.

After our description of the semisquamous epithelial layer which covers the normal gastric mucosa, and of the layer in different pathological processes, it follows logically that the criterion of ulceration should be changed accordingly. The presence of an irregular mucous membrane with a very strong infiltration of cells, will signify an ulcer only if the area of mucous membrane is not covered by a semisquamous layer, and there will not be an ulcer if this layer is present, independent of the condition of the mucous membrane. We should keep in mind that this pathology of the mucous membrane should be compared to the pathology of the skin, that is, as long as the stratum corneum is complete there is no ulceration, independent of the condition of the other strata.

Carcinoma of the stomach. The carcinomas given to us from gastric resections were far enough advanced to have given clinical or roentgenological signs which warranted their resection. For this reason, therefore, we have been unable to throw more light on the problem as to whether carcinomas always arise from an ulcer, or whether they can arise without any previous lesion of the semisquamous epithelial layer, the mucous membrane layer only, being involved. In all our studies of carcinoma, except one, we have always found large areas of ulceration, but whether these were primary or secondary we are unable to say.

As a result of our investigations we are able to describe two histological pictures of gastric carcinoma which appear simultaneously in all the carcinomas studied so far: (a) Typical carcinomatous ulcers, in which case, in the crater of the ulcer can be found carcinomatous cells. The ulcer is not protected at all by a semisquamous epithelial layer, and this is similar to the process found in the simple gastric ulcers (Fig. 16). (b) In the region between what appears to be normal mucosa and the carcinomatous ulcer, it can be seen that there are regions where the mucous membrane changes, and appears to pass from normal mucosa to carcinomatous mucosa, but the whole mucous membrane is protected by the semisquamous epithelial layer. This is the area where the carcinoma spreads toward the normal tissue (Fig. 17).

In a carcinoma which appeared to have a nonulcerative mucous membrane, we found that after formaline vapor fixation and section, that the mucous membrane was very disorganized but was covered by a well defined semisquamous epithelial layer. This layer showed areas of extensive infiltration, and in some parts there appeared to be present some very tiny ulcers of the semisquamous epithelial layer.

On the whole, this carcinoma was suggestive of a neoplastic process arising firstly from the mucous membrane itself without any previous degree of ulceration of the semisquamous epithelial layer. This is the only observation we have done, however, in which it appears that the primary lesion is in the mucous membrane, and there is only secondary involvement of the semisquamous epithelial layer (Fig. 18).

I cannot see any possibility of clearing up this problem, except for people like the medicolegalists who may be in a position to study very early carcinomas from people who have been killed by accident, and who may have

early carcinomatous changes of the mucous membrane which have not arrived at the stage of giving clinical signs. Naturally, this examination of the gastric mucosa must be carried out as soon as possible after death before autodigestion has set in.

SUMMARY

We have described the pathology of the semisquamous epithelial layer in the preulcerative processes, the absence of the layer in the ulcer itself, the aspect of the layer in the postulcerative lesion, and also how this layer is necessary in the process of cicatrization. We have studied the relation of the layer to gastric carcinoma.

Our investigations have enabled us to give evidence that the layer plays a very important part in the protection of the gastric mucosa, as without it the mucosa is destroyed, and there is a picture of gastric ulcer. The layer is absolutely necessary for the healing and reconstruction of the histology of the gastric mucosa.

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NOTES ON THE HISTORY OF RESUSCITATION IN THE MEDITERRANEAN THEATER OF OPERATIONS

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THE Mediterranean campaign lasted 30 months and was one of the longest undertaken by the United States Army since the Civil War. Tragic as this was in many ways, it did give the inestimable advantage of time, time to correct errors, time to introduce, test, and establish good practices.

THE TREATMENT OF TWO PATIENTS

Two years and many a medical *tour de force* are spanned by the following 2 cases. It is a long stretch from the Atlas Mountains, over the Apennines, to the Alps. Not only a treacherous enemy operating in a countryside always favorable to him, but mistaken concepts of treatment had to be surmounted and new procedures introduced in the slow journey that was made. There may be some value in recording why and how and when our practices became as they were at the end of the war.

TUNISIA[1]

March 21, 1943

Infantryman H. was wounded by a shell fragment and tagged at the Regimental Aid Station at 1100 hours, March 21, 1943, with the diagnosis of compound fracture of the left humerus and laceration of the left side of the chest.

First aid. Morphine, grain ½, was given at 1100 hours. Sulfanilamide dressings and a Thomas arm splint were applied. He was promptly sent to the Clearing Station where 1 c.c. tetanus toxoid was injected and 500 c.c. (2 units) blood plasma administered. His general condition was not described in his record.

Hospital entry. At some time in the afternoon he was evacuated to a Surgical Hospital. At 1715 hours his blood pressure was 110/70, with pulse of 120. More complete examination was carried out here than he had had previously. It revealed absent breath sounds and hyperresonance on the left. His abdomen was rigid and tender. At 1745 hours a further 500 c.c. (2 units) plasma injection was given. Fluoroscopy was then carried out. A fracture was found in the lower ⅓ of the left humerus with lateral bowing present. There was increased density in the left chest with the mediastinum pushed over, probably by fluid. A large foreign body was seen in the stomach region.

The chest wound was sutured. There was no evidence of "sucking."

At the time of the fluoroscopic examination the blood pressure was good and the pulse of fair quality. It was judged that the patient had a combined thoracoabdominal wound with ruptured viscus and probable hemorrhage. Transfusion and immediate operation were decided upon. One 500 c.c. blood transfusion was given. The abdomen was opened through a long left rectus incision. This was accompanied by a gush of blood and air, with

[1]From Report by Major (later Colonel) Howard E. Snyder (14).

PO VALLEY[2]

April 21, 1945

Infantryman R., age 26, was wounded by shell fragments at 1300 hours, April 21, 1945, with compound fractures of the left femur, and of both ankles, a penetrating wound of the chest with hemothorax and multiple lacerations of the legs and the face.

First aid. In the Collecting Company at 1315 hours, 1500 c.c. (6 units) of blood plasma was given, as were dressings, leg supports, and morphine, grain ¼. He was evacuated to the Clearing Station where 20,000 units penicillin were injected, 250 c.c. (1 unit) plasma was administered; and because of his exceptionally poor general appearance, 1000 c.c. whole blood was obtained from the adjacent field hospital and given. His blood pressure was 90/60.

Hospital entry. At 2100 hours. On arrival his blood pressure was not measurable, his face was pale but warm, the extremities cool, and veins collapsed. Shock was classified as severe. His blood volume was measured (see below). In the ensuing 4 hours he was given 500 c.c. (2 units) plasma and 2000 c.c. whole blood. His blood pressure had risen from 0 to 110/65; the pulse rate was 138. He received 25,000 additional units of penicillin. Operation was carried out at 0330–0600 hours, April 22 under intratracheal nitrous oxide oxygen ether. Guillotine amputation of the lower third of the left thigh was performed. Débridement was made of the extremity and chest wall wounds, with aspiration of 1000 c.c. blood from the right pleural cavity. Penicillin 25,000 units was placed in the chest. He was put on nasal oxygen. Subsequently the patient made an excellent recovery.

Laboratory notes. At 2200 hours, April 21: Hemoglobin 9.8 grams per cent, hematocrit 29, blood volume 5010. This

[2]From records of Board For The Study of The Severely Wounded (6).

TUNISIA

immediate respiratory difficulty. A 4 centimeter laceration of the dome of the diaphragm was found and closed. After this the patient's condition improved greatly. A 10 centimeter laceration of the stomach near the greater curvature was present; this was closed. It had been caused by a 1 by 1 by 3 centimeter shell fragment. The only other injury found in the abdomen was a small laceration of the spleen. This was not bleeding. Twelve grams of sulfanilamide powder was dusted into the abdomen and the incision was closed. Shortly after this the patient developed a sucking wound of the chest at the site of the entrance of the missile, previously sutured. Closed drainage was established and the wound was packed tightly with vaseline gauze. The patient died at 2315 hours, March 21.

Comment. The patient was clearly desperately wounded; he was resuscitated by 4 units of plasma and one blood transfusion. Although the blood pressure is recorded finally as normal, the pulse of rapid and only fair quality, gives evidence of inadequate resuscitation. It is impossible to judge how serious the pneumothorax was that seems to have been the cause of death or whether a bilateral pneumothorax may have been overlooked; however, the failure to surmount accidents during and soon after operation is characteristic of the bled-out patient resuscitated by plasma, without adequate blood replacement.

PO VALLEY

is 19 per cent below his calculated blood volume normal. If corrected for fluids administered he had lost since wounding 76 per cent of his normal blood volume, and 55 per cent of his normal hemoglobin.[1]

Comment. Blood plasma, 2250 c.c. (9 units), and 3000 c.c. whole blood were used here for resuscitation. (In addition, blood was used liberally in the postoperative period to overcome the acute anemia, and to promote wound healing.) Penicillin was available here but not for the earlier case. The tremendous blood loss emphasizes how dangerous it would have been in this case to have attempted to get along on plasma alone. Oxygen was available and used.

[1]While these figures are from those of the Board for the Study of The Severely Wounded (6), careful measurements of blood volume were first made in the Theater by Lieutenant Colonel John D. Stewart and Captain Frank Warner: Observation on the Severely Wounded in Forward Field Hospitals with Special Reference to Wound Shock (15).

Most of the serious problems of resuscitation of the wounded are in fact problems of the treatment of shock. Shock, in turn is a disability of the circulatory system that parallels (is caused by) loss of effective blood volume and of hemoglobin. The major problem, then, is how can this loss best be overcome, at least to the point where the patient can withstand transport to, and the necessary surgery at, the most forward hospital. The account of resuscitation as dealt with here is, broadly speaking, chiefly a history of blood volume replacement therapy in the general management of the wounded man. The history of resuscitation in this theater can be epitomized in the innovations made and their consequences, in a description of several changing trends. Some discussion of the goals sought and the errors it became necessary to avoid will clarify the reasons for the innovations.

While differences in terminology, in organization, in evacuation, in resources technical and human vary so from World War I to World War II, comparisons are in most cases useless; however, the organization and mission of Field Hospital 127, in France in 1918, are said to have been comparable to that of the 33rd Field Hospital in the Mediterranean Theater in 1943; so the following table can be used for the valid illustration of a point:

	Field Hospital 127 1918	Field Hospital 33 1943
Number of days included	7	30
Cases admitted.....	256	297
Deaths without operation	41	0
Deaths after operation..	34	56
Total mortality rate....	29.3 per cent	18.8 per cent
Operative mortality rate.	15.8 per cent	18.8 per cent

The interesting point in the table is the fact that all patients were prepared for operation in the 1943 group, whereas 41 or 16 per cent never were considered to be ready for surgery and died without operation in 1918. There are chances for serious error in this type of comparison, but there can be no doubt that striking differences in surgical management are illustrated here, and that the key to these is resuscitation.

GOALS SOUGHT

The final statement in Dickinson Richards's Harvey Lecture says, "The greatest mis-

take is to suggest, as some have done, that shock is a problem that has been solved." (Certainly few therapeutic attempts can be said to be completely successful.) Dr. Richards's point is a sensible one; but there is another view that must be considered as well. In the report of the Board for the Study of the Severely Wounded, the statement is made, ". . . the results (of this study of battlefield casualties) have shown in a useful way what appears to be a quantitative relationship between blood loss and degree of shock, long recognized, but always in need of all the support possible in order to outride the ever recurring storms arising from suggestions that the cause of shock is mysterious and to be explained by toxins or the breakdown of some vague but vital force." To recognize the relationship of blood loss to degree of shock as a practical guide in treating patients is not to minimize the interest or the importance of the shock problems awaiting study, nor is it to underestimate the complexity of the mechanisms involved in the production of shock; but it is to emphasize the importance of applying the therapy we know to be effective. Too much preoccupation in the clinical treatment of patients with the unsolved problems of shock can have the indirect but very closely associated result of leaving the physician without access to adequate necessary equipment for applying the therapy well proved to be effective in the treatment of shock: blood as needed. This was the unfortunate fact in Tunisia.

A shrewd estimate of the extent to which the patient has suffered from his wounds (15) is necessary for a correct appraisal of the therapy needed in order to enable him to withstand transport to the forward hospital. Once there, his response to the journey and to subsequent therapy will give valuable information as to what support he needs to withstand the surgery necessary. When the patient has been rescued from the condition where organic damage may occur as a result of inadequate circulation, a very important element in his care lies in the correct timing of resuscitative measures and of operation. These matters have been discussed by Beecher and Burnett, 1944 (5), and by Beecher (3), 1945. Lalich (10) and Lalich and Mason (11) in detailed reports described careful studies to aid in appraising the patient's condition and to guide in determining quantity and timing of fluid therapy as well as timing of operation.

INNOVATIONS AND THEIR CONSEQUENCES: TRENDS

Plasma.[1] The early difficulties of resuscitation in Tunisia (described below) are directly attributable to a mistaken concept of the limits of usefulness of human blood plasma. While there is no need to dwell upon this fact, long since corrected, any account of resuscitation would not be complete without some reference to it.

A misconception: The use of plasma was suggested by Ward (1918) during the last war; but the agent did not become available then. Presumably this suggested use grew out of the belief that the method of blood transfusion then available, plus the hazards involved, offered too great obstacles to the widespread use of whole blood for resuscitating battle casualties, hazards that were too great to be allowable.

In Ward's communication (19), which was in the form of a letter to the editor of the *British Medical Journal*, he said, "There is abundant clinical and experimental evidence that it is not the corpuscles that are wanted, but the ideal fluid for keeping blood pressure at the proper level. . . . A man dying from hemorrhage is not dying from lack of hemoglobin . . .but from draining away of fluid, resulting in devitalization and low blood pressure."

These incorrect remarks were followed by the sensible suggestion that trial of plasma should be made and *controlled with the same number of whole blood transfusions.* Apparently this was not done.

Plasma[2] was recommended in 1939 as "an ideal substitute for whole blood in the emer-

[1] This article was written in Italy with little possibility of checking the references. All care possible has been taken to insure accuracy of quotation of spirit as well as of word. If error of fact or wrong emphasis has been made in the references given, this can be attributed to the circumstances, and is deeply regretted by the writer.

[2] While one might have concluded from reading much of the literature of the period that the importance of hemoglobin had been forgotten, this was not everywhere the case. For example Kilduffe and DeBakey (9), emphasized the importance of hemoglobin (p. 277).

gency treatment of shock and hemorrhage from war wounds," by Tatum, Elliott and Nasset (17). Many other references could be given along this same line; but there is no reason to do so. The changed point of view has been so well summarized by De Bakey and Carter (8), it may be quoted here rather fully:

"Although the development of plasma has undoubtedly been a great contribution, its usefulness in shock therapy can now be viewed in proper perspective. Unfortunately, the early enthusiasm that accompanied this development was so forceful that it pushed aside sound clinical judgment and led to the widespread misconception that plasma could be used as an effective and complete physiologic substitute for whole blood in the management of shock in the seriously wounded. This misconception became so firmly entrenched in the minds of both administrative and professional personnel that it somewhat handicapped the organization and development of more effective measures for the management of shock. With increasing experience in the treatment of shock, it became more and more evident that plasma could not be used as a complete substitute for whole blood. It was found that while seriously wounded men could be brought out of shock with plasma, they were frequently unable to withstand the life-saving surgery that was subsequently necessary. Superficially, such patients appeared ready for surgery, but it was soon realized that this appearance gave a false sense of security for even movement of the patient, anesthesia, and other procedures in preparation for surgery often caused the patient to fall back into shock. It soon became evident that whole blood transfusion was essential for the proper resuscitation of these patients and that whole blood is the only therapeutic agent that will prepare seriously wounded patients to withstand the surgery that is essential for the saving of life and limb."

The now widely recognized misconceptions that plagued the early *use of plasma* should by no means obscure the remarkable value of the substance as a life saving innovation. It has superbly filled the need of supporting life while the patient is transported to a place where whole blood transfusion is feasible. It also is useful where blood concentration is present, chiefly in burns, in crushing injuries, and in some abdominal wounds. The shifting emphasis in the use of the agent is shown in the following section.

Plasma and whole blood. A detailed consideration of these agents will be presented by Lieutenant Colonel Eugene R. Sullivan in a history of the base blood bank. He also will present a description of the available equipment for transfusing blood, its inadequacies and shortages in the early Tunisian campaign, responsible in part for the relatively infrequent use of whole blood during that period. A few sample figures may be given here.

In general, the records of the use of plasma are too inaccurate to justify detailed presentation. A few dependable samples of these are:

Use of plasma in the Tunisian campaign is shown in the following II Corps report for the period, 1 February to 31 March 1943: number of casualties needing plasma, 972; per cent of casualties needing plasma, 34.3; unit consumption per 1000 for the period, 320.

In a sample of 431 *seriously* wounded men admitted to the hospital in the II Corps, January 21, 1943 to February 28, 1943, 101 patients received plasma (total quantity not stated), and 31 blood transfusions were given, In March, 561 patients were admitted to Surgical Hospital No. 48; 741 operations were carried out; 97 whole blood transfusions were given.

These data contrast with the following, also from seriously wounded patients (6). Preoperative blood plasma, 3.08 units per man (based upon an average of 122 cases); blood plasma given during operation, 1.68 units per man (based upon an average of 10 cases); preoperative whole blood, 1450 c.c. per man (based upon an average of 127 cases), blood given during operation, 1160 c.c. per man (based upon an average of 95 cases).

The average of these very seriously wounded patients thus received from the time of wounding until the end of operation 3 to 4 units of plasma plus 5 blood transfusions.

In a letter written by Lieutenant Colonel (now Colonel) Frank Berry, surgical chief of the 9th Evacuation Hospital to the Surgeon of the North African Theater of Operations on July 1, 1943, the following data are of interest.

Date	Number of battle casualties treated	Number of blood transfusions given	Ratio of transfusions to battle casualties
March 1943	1146	17	1: 67.4
April 1943	1558	54	1: 28.9
May 1943	397	27	1: 14.7

This remarkable trend continued. In an average of the data from 8 evacuation hospitals for the first 100 days of the Italian campaign, beginning September 9, 1943, the ratio of transfusions to battle casualties was 1: 4.5. For all Fifth Army Hospitals for January, 1944, the ratio was 1: 2.4. The base blood bank was introduced in February, and in March the ratio had changed to 1: 1.9. The trend is rather strikingly shown in the figure. The rapid rise in the incidence of the blood used was due to two main factors: (a) realization that plasma alone was not adequate and that whole blood was necessary, and (b) increasing availability of the necessary organization and equipment for transfusion. The undramatic change shown between January and March of 1944, during which time the base blood bank began to function (February 23, 1944), does not justly characterize this important innovation. While it is true that blood in large volume was being obtained before the base blood bank was established, from local institutional blood banks, from local emergency bleeding as needed, and by borrowing from the British, the generally greater safety and uniformity of the blood after the establishment of the base blood bank is, of course, not shown in a graph such as Figure 1. Moreover, the ready availability of very large volumes of blood, up to several liters, for a given case is a very important consequence of the introduction of the base blood bank, emphasized by Lieutenant Colonel Sullivan's (16) observation that in the first 100 days of the Italian campaign the field hospitals cared for one-thirteenth of the battle casualties and used one-third of the blood. A few of the very badly wounded used a disproportionately great volume of the blood.

Albumin. Albumin was first used in the field in this theater by Beecher and Burnett 1944 (5). In some 200 patients no definitely significant untoward effects were observed. As expected on the basis of clinical trials in the United States, low blood pressure was elevated, although transiently, by the albumin. Clinically, one unit of albumin was found to be about comparable to one unit of plasma in its blood pressure elevating effect, notwithstanding the theoretically greater power of the albumin. The chief advantages of this agent center around its small bulk and ready availability, for use in difficultly accessible situations where space and weight are at a premium.

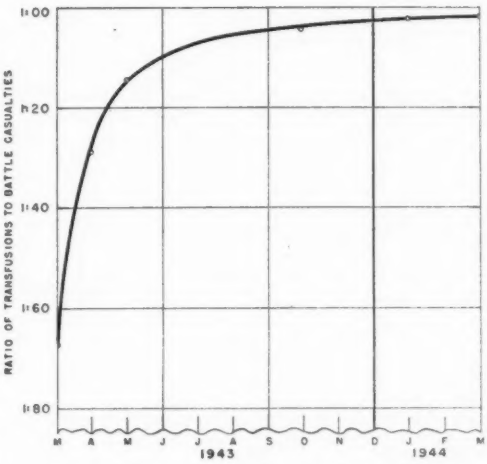

Fig. 1. Showing increasing use of whole blood.

"STABILIZATION" VERSUS RAPID PREPARATION OF BATTLE CASUALTIES FOR SURGERY

At about the time of the crossing of the Volturno River, when the fighting was quite heavy below Venafro, early in November, 1943, a new point of view began to appear in the shock tents of the Fifth Army, to the effect that too much urgency was exercised in the preparation of the wounded for surgery. After 2 or 3 months this view had lost its negative character and during the prolonged fighting before Cassino, in the early months of 1944, it came to be stated in a positive way. In effect what was said was this: "The wounded get along better if surgery is delayed, even after the blood volume and hemoglobin and blood pressure have approached normal." Patients were said to profit by something vaguely described as "equilibration" or "stabilization." What it was that happened merely with the passage of time was never very clearly defined. "They just did better." And, of course, there is some basis for such a view, although hardly as it came to be em-

ployed. Anyone could see that seriously wounded men who had been bounced over rough roads in a long ambulance haul, resting poorly, often in great pain as the result of movement, frequently arrived with rapid, weak pulse, and low blood pressure. With nothing more than 10 or 15 minutes of rest, the blood pressure would rise and the pulse improve in quality. The chief gains to be obtained by rest at this stage of the patient's treatment are usually achieved in about 15 minutes. On the other hand, as stated elsewhere (3):

> ". . . . the wound has set several continuing processes in action; there is bleeding and plasma loss from serous surfaces and into traumatized tissues. Contamination leads to progressing infection. With these and other drains upon him, the seriously wounded patient must have constant external support by way of blood and plasma. If, as a principle, one can say that the smallest quantity of blood and plasma should be used that is compatible with the patient's well being . . . then early operation appears desirable on this basis. Unquestionably, delay in operation necessitates the use of larger quantities of blood and plasma to maintain the patient on an even keel than otherwise is the case. A further point is important in this connection. It has been well established in the cases of peritoneal contamination encountered in perforated peptic ulcer that the mortality rate rises sharply with the passage of time. With the grosser contamination met in warfare this is probably also the case. The passage of time is against the patient's good."

Beecher and Burnett, 1944 (5) proposed, following a study of 2853 battle casualties at Cassino and Anzio from which the shock cases, 72, were filtered, that surgery be undertaken as early as possible, and as arbitrary guides suggested that when the blood pressure is swinging up and is not below 80 millimeters of mercury systolic and the pulse rate falling, if the patient's skin is warm and of good color, that he be taken at once to surgery and whatever further blood administration is necessary be given during surgery, *surgery being considered an integral part of resuscitation.* The results of this policy in the 2853 patients referred to were excellent, and while the proposal caused considerable discussion and disagreement at first, it has gradually come to be accepted as a satisfactory general working principle.

ERRORS TO AVOID

Any history of resuscitation in this theater would not be complete without some mention of the errors it was found necessary to avoid. The usual ones involved in poor medical care need not be reviewed here, such as poor splinting, inadequate protection from weather and so on, rather several things will be mentioned here that are either new or have received new emphasis in the campaigns in this theater.

Morphine overdosage. It very early became apparent in Tunisia that the half-grain (30 mgm.) morphine *syrette* was *too large.* Medical corpsmen in this campaign were permitted to administer morphine for the first time in the history of the United States Army. While some have attributed the difficulties with the half-grain morphine syrette to this fact, it was the general observation that medical officers seemed more often to be at fault in their overuse of morphine than were the men.

In the cold, wet, early days of November 1943, it was repeatedly observed (2)[1] that patients whose peripheral circulation was sluggish as a result of either chilling or low blood pressure, absorbed subcutaneous or intramuscular injections of morphine slowly or not at all. This *delayed morphine absorption* too often led to the conclusion that the patient, who naturally got no effect from the unabsorbed morphine, was "resistant" to the drug and a second or third half grain was injected. This added drug had disastrous consequences when simultaneous and rapid absorption of all of the morphine injections occurred after the peripheral circulation was re-established as a result of resuscitation and the application of warmth.

The Surgeon of the Fifth Army established the rule, late in 1943, that corpsmen were not to administer more than half of a morphine syrette. In addition to this, a vigorous educational program and the appreciation of the possibilities of delayed morphine poisoning all led to a sharp reduction in the accident of overdosage.

In a study (4) carried out chiefly on the Anzio beachhead, it was found, on the basis of an extended factual inquiry, that severe pain

[1]This had also been pointed out a year earlier in a civilian disaster, (Cocoanut Grove). *Ann. Surg.*, 1943, 117.

is much less common in the severely wounded than had been supposed, and that those who wanted (in response to a direct question) further pain therapy, even though no morphine had been administered for several hours, were surprisingly few. It was observed that certain wounds, notably penetrating abdominal wounds, are far more painful than others; but that morphine is as likely to be given to a patient with little pain as to one with severe pain. The observation was made and subsequently confirmed throughout the Theater that the severely wounded are often in need of sedation of the barbiturate type, that the use of a modest dose of a barbiturate will control in some cases manic behavior formerly attributed to pain, and in many cases will obviate the need for morphine. As a generalization, the wounded were found to need small doses of both a sedative of a barbiturate type and of morphine. It was found that *this combination would often accomplish what large doses of either agent alone would fail to do.*

Delay in evacuation. It was not until in the Italian campaign that it came to be *generally* appreciated that too much time was consumed and too much handling of the patient undertaken by the too frequent insistence on an out-of-the ambulance checking of the patients at each stop along the evacuation trail. Not enough by-passing of some installations was carried out in order to expedite the passage of the wounded man to the hospital where he could get emergency surgery. This problem is difficult to solve with the present evacuation system. Various suggestions have been made that this be critically reviewed and modified in the light of experience. It seems inevitable that men of little clinical experience must staff the forward (the collecting company, the clearing station) installations. Perhaps something can be accomplished by education. It is more likely that a major step toward solution of the problem will occur only when the opportunities are reduced for these young and eager men to exercise their, in some cases, not yet adequately trained judgment, that is, only when one of the way stations is eliminated.

The rather constant average of a 5 hour interval from hospital entry to surgery in the case of the seriously wounded seems too long. It was shown (5) that this could be reduced to 2⅓ hours, but in general not enough progress was made in cutting down this time.

Overuse of plasma preceding hospital entry. Notwithstanding earlier views to the contrary, the truly vital importance of hemoglobin has been established. The administration of plasma preceding hospital entry beyond the point where the blood pressure is elevated enough to get the patient out of the critical shock level, will lead to renewed bleeding and perhaps critical loss of hemoglobin. Resuscitation by plasma alone can give a false appearance of well-being in the patient and a false sense of security in his doctor, preserved as long as the patient is not subjected to any strain. The true weakness of the patient was often revealed in the early part of the Tunisian campaign (where large volumes of plasma were used without adequate blood transfusion), as soon as any strain was put upon him, such as that due to anesthesia and operation.

STUDIES INSTITUTED WITH A VIEW TO IMPROVING THE RESUSCITATION OF THE WOUNDED PATIENT

These studies can be grouped under five headings; they have been reported in detail elsewhere.

The laboratory and clinical studies of Lieutenant Colonel John D. Stewart and Captain Frank Warner (6), those of Captain Joseph J. Lalich and Major James M. Mason, III (10, 11), those of Lieutenant Colonel Henry K. Beecher and Major Charles H. Burnett (5, 7), the observations of the Board for the Study of the Severely Wounded,[1] and finally the observations that grew out of astute clinical observation alone, for example, those of Major Luther H. Wolff and Captain Trogler F. Adkins (20) on tourniquets and Major Luther H. Wolff and Captain Robert D. Beech (1) on gastric dilation.

Less planned but equally important to the patient's welfare were the countless and inspiring examples of ingenious resourcefulness and devotion to the patient's well-being shown on all sides. Examples of these impromptu

[1]Members of Board: Lieutenant Colonels Tracy B. Mallory, Fiorindo A. Simeone, Henry K. Beecher, and Eugene R. Sullivan, Major Charles H. Burnett, Captains Seymour L. Shapiro, and Louis D. Smith.

studies are too numerous to describe; but one or two may be mentioned. Captain William Weiss's efforts to devise an apparatus whereby air or oxygen could be administered under positive pressure was one example from the early days in Tunisia. His efforts to devise a satisfactory suction apparatus were finally successful when he passed a tube from the operating tent to the windshield-wiper of a truck parked outside. Justly celebrated was Captain Werner Hoeflich's preoccupation with any wrecked airplane that he could get his hands on, in order to get the parts necessary to build a workable positive pressure apparatus to be used in conjunction with a breathing bag (basket ball bladder) he had obtained. Captain W. R. Turnbow made many ingenious improvisations for the care and safety of the patient in the operating room.

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EDITORIALS

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THE VALUE OF RED CELL TRANSFUSIONS

THE large scale preparation of plasma during the recent war made available considerable quantities of red cell residues. The value of red cell transfusions in the treatment of anemia was recognized first in England and later in this country. Through the Blood Donor Service of the American Red Cross, red cell suspensions were distributed without cost to civilian hospitals in several urban centers. Over 15,000 red cell transfusions were given in the Detroit area alone. Red cells were also generally obtainable and had wide use in hospital blood banks where plasma was processed. Through these experiences, red cell transfusions for the treatment of anemia have become a well established therapeutic procedure.

Red cells may be given in their concentrated form or isotonic saline solution equivalent to the amount of plasma withdrawn may be added. The hematocrit of a concentrated red cell suspension averages 85 to 95 per cent which means that about 10 per cent of the plasma remains behind. This is sufficient to allow such a suspension to run freely through an 18 or 19 gauge needle. The flow is facilitated by raising the height of the suspension and by occasional agitation. Because of the small amount of plasma present, concentrated type O cells can be given safely to recipients of any blood group. As a precaution, the recipient's serum should always be matched against the donor's cells before use. Some authors have pooled the cells from two or three type O donors thus giving the recipient a large transfusion without changing bottles. Red cells remaining from blood that has been drawn into citrate solution should be used within five days. It has been shown that addition of a 10 per cent solution of corn syrup will preserve red cell suspensions for 14 to 21 days.

The main indication for the use of red cell transfusions is to raise the oxygen carrying power of the blood in patients with anemia. When anemia is associated with shock or hypoproteinemia, whole blood certainly is to be preferred. In such cases, however, red cell suspension supplemented with plasma should produce the same effect as whole blood. Toward the end of the war, the superiority of whole blood over plasma in the emergency treatment of hemorrhage with shock became well recognized. In this regard, it is interesting to note that, in recent experiments on dogs, red cell suspensions were more effective than plasma in overcoming shock produced by a single large hemorrhage.

For the treatment of anemia, red cell transfusions are as effective as an equivalent amount of whole blood. A similar rise in the erythro-

cyte count and hemoglobin value occurs and the survival period of the cells are the same with both types of transfusion. In many of the reported series of cases, the percentage of adverse reactions are somewhat lower with cells than with whole blood.

There are certain advantages of the transfusion of red cell suspensions over whole blood. Probably the chief advantage is the factor of economy. Blood obtained from professional donors has always been expensive and the supply from friends and relatives is often limited. Thus many patients do not receive the amount of blood necessary to restore the erythrocyte count to normal during periods of stress. As there will continue to be a demand for human plasma, it would seem desirable to divide the cost of whole blood between the plasma and red cells. Both products would then be more available to low income patients. Another advantage of red cell suspensions is the fact that type O cells can be given to recipients of any blood type. Type O whole blood with a high agglutinin titer in the serum is a potential source of danger when used universally. The reduced volume of concentrated red cell suspensions as compared to the original volume of the whole blood from which it is obtained also has advantages. The cells from one to two liters of blood can be given over a period of several hours thus causing rapid and marked increases in the erythrocyte count. In some cases it is desirable that sufficient blood be given to raise the erythrocytes and hemoglobin to normal over a short period of time. The danger of overloading the circulation is an important consideration in patients with cardiac disease or with anemia alone. Deaths due to cardiac failure may result from the rapid administration of blood to a severely anemic patient. This danger is lessened with the use of concentrated cell suspensions.

In the average hospital, over half of blood transfusions are given primarily for the treatment of anemia. These patients would benefit equally from red cell suspension transfusions. Because of the expense and unavailability of whole blood, it is not uncommon for sick patients to receive only one or two pints of blood regardless of the degree of anemia. If red cells were available at a low cost, they could be used more freely than is the present practice with whole blood. Preoperatively and postoperatively, the erythrocyte count and hemoglobin level could be maintained at normal levels regardless of the amount of cells required. In patients with iron deficiency anemia the hemoglobin can be raised rapidly with cell transfusions; as the transfused cells die off, the iron released becomes available for the formation of new erythrocytes. Spontaneous recovery of the anemia following hemorrhage or the recovery of pernicious anemia with liver therapy requires about six weeks. Convalescence is greatly hastened in such cases by the transfusion of the red cells from one or two liters of blood. Red cell transfusions are ideal for patients with aplastic anemia and other blood dyscrasias where the rate of blood formation is less than that of blood destruction.

It is needless to say that red cell transfusions just as whole blood should be given only when clear cut indications are present. In individuals over 60 years of age, erythrocyte counts of 4.0 million and hemoglobin values of 12 grams fall within the normal range. Nothing is to be gained by raising the erythrocytes and hemoglobin over these levels. By so doing, the tendency to cardiac embarrassment and thrombosis is increased. Patients with a low grade static anemia as from sepsis or azotemia are probably little benefited by temporarily raising the red blood cell count. The dangers of transmitting hepatitis, malaria and syphilis are present with cell suspensions as with whole blood.

At the present time, red cell suspensions are not easy to obtain. The discontinuation of mass blood donation to the armed forces for the processing of plasma has eliminated this source of cells. Further, Red Cross lyophilized plasma has been given to civilian hospitals throughout the country. Therefore, there is little demand for fresh plasma from which the red cell residues ordinarily would be available. When the present supply of Red Cross plasma is exhausted, there undoubtedly again will be an extensive processing of plasma and the red cells can be salvaged. The increasing use for various protein fractions from human plasma is another potential source of red cells. When red cell suspensions again become more plentiful, they deserve general usage in the treatment of anemia. HOWARD L. ALT.

ANEMIA IN BURNS

WITH the treatment of burns becoming sufficiently advanced to make it possible to keep the deeply and extensively burned patient alive, the anemia of burns is being encountered more frequently and of a severity often incompatible with life. Previously accepted as rare and of little concern, it has emerged from obscurity during the period of war research to be defined to the extent that it should be predicted and forestalled.

As a result of recent study of the anemia of burns, more causes for it have been found than were heretofore considered. To external blood loss have been added the effect of heat upon the circulating red cell, the internal disappearance of cells presumably the result of widespread infection, and inhibition of red cell regeneration. The obvious loss of blood from the granulating wound surfaces[1] and the occasional finding of blood in the stools[2] had made it reasonable to ascribe the anemia to external blood loss. The presence of hemoglobinuria in victims of the Cocoanut Grove fire suggested to Shen and Ham[3] the probability of an internal breakdown of red cells as well. In these and subsequent patients they observed an increased fragility and abnormal spheroidal shape of the circulating red blood corpuscles. On the basis of experimental evidence in human and dog blood these abnormalities were ascribed to the effects of the heat upon those cells circulating in the periphery.

The findings of Shen and Ham have been elaborated by Brown of the Burns Unit under Colebrook at Glasgow[4]; the increased fragility of the red corpuscles was found to be limited to the hours immediately following the trauma. The increase was gradually supplanted by a subnormal fragility which lasted until the tenth day; the normal level of fragility was passed at the thirty-sixth hour. The subnormal fragility was ascribed to the disappearance from the circulation of the more fragile cells. It was postulated from experimental observation that the volume of cells hemolyzed could amount to as much as 8 per cent of the original number present before trauma. The hemolysis of fragile cells was also correlated with the extent of the burn. Although increased fragility was found in patients with less than 15 per cent of the body surface burned, it was only in patients with burns of more than this extent that a decreased fragility and a subsequent anemia were discernible.

An internal disappearance of red cells has also been demonstrated beyond that which can be accounted for by the hemolysis due to the burn trauma. Investigators of the Har-

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[4] COLEBROOK, L., *et al.* Studies of Burns and Scalds (Reports of the Burns Unit, Royal Infirmary, Glasgow, 1942–43), Medical Research Council, Special Report Series 249. London: His Majesty's Stationery Office, 1944.

vard Medical School and the Massachusetts Institute of Technology, using precise methods for determining the red cell mass and pigment excretion, have observed a massive disappearance of red cells in deeply and extensively burned patients in the first two months after injury[1]. The maximum loss observed was 318 cubic centimeters of packed red cells per day for the six days following injury. This loss was observed in a healthy young woman with a burn of 78 per cent of the body surface, 45 per cent of the surface being of full thickness destruction. From the fiftieth to the seventy-second day this same patient was found to be losing cells again and at the rate of 65 cubic centimeters of packed cells per day. Another severely burned patient, from the tenth to the eighteenth day after injury, lost 191 cubic centimeters per day, and from the nineteenth to the thirty-sixth day, 74 cubic centimeters per day. The internal disappearance was not observed in patients with extensive partial thickness or only circumscribed full thickness burns, and, unexpectedly, not in two elderly, deeply and extensively burned patients who did not die until the eighth and tenth days after injury.

The origin of this internal loss or disappearance of red cells is obscure but since it appears only in patients with extensive deep burns, it is tempting to ascribe it to the infection of mixed organisms characteristic of the full thickness burn wound allowed to lie fallow and separate its slough spontaneously. That it is not due to the trauma sustained by the red cells at the time of the burn is proved by the observation that cells transfused into the patient after the injury partake equally in the disappearance. For this determination tagged cells were used prepared by injecting volunteer donors with radioactive iron.

The fate of the vanishing red cells is also obscure. Although an excess of urobilinogen was found in the urine during the periods when the red cell mass was observed to be shrinking, the excretion products of blood pigment accounted for but 10 per cent of the loss. The recent work of the Menkins[2] and of Wintrobe and his collaborators[3] suggests that the red cells and hemoglobin may be disintegrated at the inflammatory barrier.

The possible failure of red cell regeneration as a contributing cause of the anemia has also been explored by injecting radioactive iron into the burned patients.[4] The rate of red cell formation was judged by the rise in the level of radioactivity of the circulating red cells. In an unburned normal person 70 per cent of the radioactive iron injected is elaborated into the hemoglobin of the circulating cells at the end of eight days. In a patient with a severe burn the red cell formation may be reduced to less than a third of the normal.

The early anemia due to initial hemolysis and massive internal red cell disappearance must be differentiated from the pseudoanemia of hemodilution which occurs from the third to sixth day after injury. The pseudoanemia is due to an enlarged plasma volume and results from a resorption of wound edema at a rate in excess of renal excretion. The distinction between the true and false anemias is important from the point of view of therapy.

The treatment of the true anemia of burns is whole blood transfusions; the circulating red cell mass should be maintained as nearly replete as possible at all times. The treatment of the false anemia of burns is the curtailment

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of fluid therapy. Transfusion of the patient with a false anemia results in a further increase in blood volume and the danger of cardiac insufficiency and pulmonary edema. In the effort to forestall the true anemia of the extensively and deeply burned patient it is tempting to inject large volumes of whole blood in the first days after injury with the understanding that the blood given in the initial hours would be a part of the therapy for the burn shock. Whole blood and saline solution instead of plasma have been recommended by Moyer and associates for the treatment of burn shock[1]. Should the anticipated red cell destruction and anemia not be realized, however, the excessive red cell mass will prove embarrassing. To ascertain, therefore, whether whole blood is indicated, periodic measurements of the plasma volume and red cell mass are required. The dye technique for these measurements is simple, accurate, and well established; the hospital caring for burn patients should provide the surgeon with this laboratory aid.

Although we are able to predict and forestall the anemia of burns, we still do not know how to preclude the continued red cell disappearance. Because the infection of the wounds is possibly an instrument of red cell destruction, expeditious closure of full thickness wounds and administration of polyvalent chemotherapy are not amiss. OLIVER COPE.

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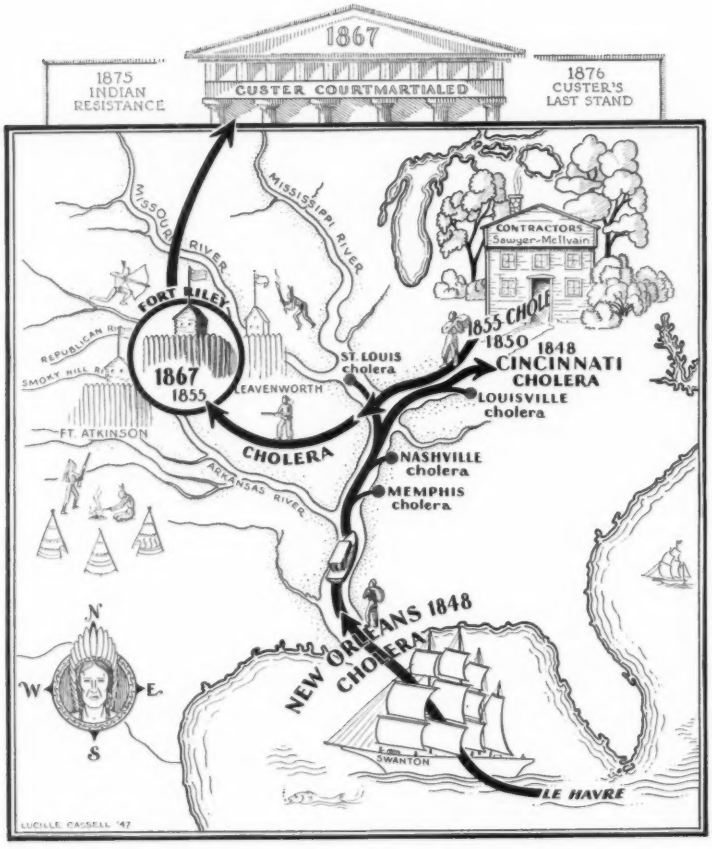

Did Cholera Defeat Custer. — *Paul R. Hawley.*

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DID CHOLERA DEFEAT CUSTER

PAUL R. HAWLEY, M.D., Major General, U.S.A., (Ret.), Washington, District of Columbia

ON October 31, 1848, the Swanton sailed from Le Havre with 280 steerage passengers, most of them German emigrants, and arrived in New Orleans on December 11, having lost 16 of her passengers en route with an intestinal complaint. She proceeded directly to her dock and discharged cargo and passengers. The next day one of the surviving passengers was admitted to Charity Hospital with a frank case of Asiatic cholera. Other cases followed in rapid succession, the disease spreading among the inhabitants of the levee district. In less than 2 weeks there were from 40 to 50 deaths from cholera per day in New Orleans.

Within an incredibly short time practically every packet boat on the Mississippi River was infected, and the epidemic spread to Memphis, St. Louis, Nashville, Louisville, Wheeling, and Pittsburgh. On Christmas day, 1848, victims of the disease were removed from a river boat in Cincinnati and taken to the General Hospital. During the winter weather sporadic cases occurred among the local population in Cincinnati; but, when the weather turned warmer in Spring, the disease burst forth in epidemic violence, to disappear in the Autumn. It reappeared in June, 1850, but with diminished fury.

For more than 25 years after the opening of the Santa Fe Trail in 1822, hostile Indians menaced its travelers. Along its middle reaches in what is now the State of Kansas, the Pawnees were the fiercest; but the Kaws, who inhabited the valley of the Kansas River (about and north of the location of present Council Grove), while not warlike, were assiduous cattle thieves and made frequent raids upon the wagon trains passing through their locality.

Fort Atkinson was established in 1850 on the Arkansas River about 6 miles above the site of the present Dodge City. Its garrison afforded some protection in Southwestern Kansas, but the nearest Army post to the east was Fort Leavenworth, on the Missouri River, almost 400 miles distant by trail. The Kaws, therefore, were relatively free to plunder unguarded wagon trains.

The discovery of gold in California greatly increased the traffic over the Santa Fe Trail; and the thievery of the Kaws grew apace. Being unable to protect this section of the trail from his base of operations at Fort Leavenworth, the Commanding Officer of the First Dragoons recommended to the War Department, on July 31, 1852, that another Army post be established "at or near a point on the Kansas River where the Republican fork unites with it." Acting upon this recommendation, the Secretary of War, Mr. Jefferson Davis, directed that a Board of Officers be appointed to select the site for a new post in the vicinity of the fork of the Kansas River; and, late in the Autumn of 1852, a company of the First Dragoons escorted this Board to the spot where the Smoky Hill and Republican Rivers join to form the Kansas River.

It is interesting to note in passing that the temporary camp pitched there was named "Camp Center," because these officers knew, at that early date, that they were not far from the geographical center of the United States. That the Coast and Geodetic Survey of the United States was sufficiently accurate in 1852 for such a close approximation is surprising. For many years the monument marking the geographical center of the United States stood within the easy throw of a stone from the junction of the Smoky Hill and the Republican Rivers; but later refinements in the survey have located the point about 100 miles away.

After the favorable report of the Board was approved, and money was appropriated by the Congress, the construction of temporary buildings was begun at Camp Center. After the death of

Major General Hawley is Chief Medical Director, Veterans' Administration.

Brevet Major General Bennett Riley, in June of 1853, the new post was given the name of Fort Riley. The Congress that adjourned on March 3, 1855, appropriated funds for the expansion of the post with permanent buildings; and the contract for this work was let to the firm of Sawyer and McIlvain, of Cincinnati. This firm prepared the millwork, procured the hardware and collected the artisans in Cincinnati, and shipped all by river boat to Fort Leavenworth, whence they were transported to Fort Riley by wagons. The Board had reported an ample quantity of good building stone at the site.

Work commenced on the new construction early in July, 1855. Before the end of the month there were 2 deaths from a disease very like cholera. On the first of August the epidemic began in earnest. There were several deaths each day and the presence of Asiatic cholera was no longer in doubt. Panic seized the camp. The Constructing Quartermaster died of the disease. Workmen opened his safe with explosives, divided among themselves the gold it had contained for their pay, and scattered over the plains. The Army doctor, fearing for the safety of his wife and family, deserted his post and drove away with them in an ambulance. For this he was tried by court-martial and dismissed from the service.

The epidemic burned itself out rapidly, its fuel being depleted by death and desertion. Convalescents regained strength and were reinforced with new recruits from the East. Work was resumed and the post completed without further incident. Some of the survivors of the epidemic remained as permanent employees of the post.

George Armstrong Custer was graduated from the United States Military Academy on June 24, 1861, at the age of 21 years, and was commissioned a Second Lieutenant, of the Second Cavalry, United States Army. Less than two years later he was a Brigadier General; and within another year was a Major General, commanding a Cavalry Division.

The surrender at Appomattox found Custer, not yet 27 years old, a major general whose only future in the Army was a garrison life on a frontier post with occasional brushes with small bands of Indians. At that he fared far better than many of his older comrades who had served with distinction in the war. One of the new Regular regiments created in the reorganization of the Army was the Seventh Cavalry; and Custer was given the permanent grade of lieutenant colonel of this regiment—a grade which often required 30 years to reach in the peace-time Army. Furthermore, the colonel of this regiment was employed almost all the time on detached service, and Custer held uninterrupted command of the regiment.

Until the Spanish-American War the Army maintained the system of brevet rank in lieu of medals for distinguished service. The only military decoration was the Congressional Medal of Honor; and achievements not warranting this decoration, and some that did, were recognized by conferring a brevet rank upon the officer. A brevet rank was, for practical purposes, only an honorary rank. Thus a captain could be brevetted, for successive deeds, a major, a lieutenant colonel, and even higher, while remaining a captain. His command authority continued to be that of a captain, but he took precedence among captains by virtue of the date and grade of his brevet rank.

With his reduction to the permanent rank of lieutenant colonel in the demobilization of the war-time Army, Custer retained his brevet rank of Major General. It is necessary to remember this in order to understand the administrative maneuvers that occurred when the selection of a commander for the expedition against the Sioux was under consideration.

The year 1867 found the newly organized Seventh Cavalry stationed at Fort Riley, Kansas, under the command of Custer. Garrison routine was broken by occasional forays against hostile Indians. Custer employed the slashing cavalry tactics of the period and was uniformly successful—on the surface, at least—in his encounters with Indians. His favorite method of attack was a mounted charge through the Indian camp, launched before the warriors had recovered sufficiently from the surprise approach of the troops. It has been alleged that rarely was a living creature—braves, squaws, or papooses—spared in these encounters.

During the summer of 1867, when the Seventh Cavalry was on an Indian-hunting expedition in what is now Western Kansas and Eastern Colorado, Asiatic cholera again broke out in Fort Riley. There was the usual panic that accompanied the appearance of this terrifying disease. The news reached Custer in the field, and he became alarmed over the safety of Mrs. Custer who was living at Fort Riley.

Upon his own authority, he left the regiment in command of the next senior officer; and, with an escort of 100 troopers, Custer set off post-haste in a mule-drawn ambulance for Fort Harker, near the site of present Ellsworth, Kansas, whence he boarded a train for Fort Riley. For this violation

of the Articles of War, charges were preferred against Custer and he was ordered to appear for trial by a general court-martial.

The initial charges were that he had, without authority, left his command—in other words, had been AWOL. But now that the hitherto untouchable favorite of higher commanders had made himself vulnerable, past offenses—the knowledge of which had rankled in many breasts for some months—were brought to light. Additional charges were preferred. It was alleged that, during the dash across the plains to Fort Harker, his small rear guard of troopers had been attacked by Indians and that he had pushed on without sending assistance back to them. There were casualties and the question was raised as to whether or not some of the living troopers did not fall into the hands of the Indians.

It was an unpardonable sin, in the unwritten code of Indian warfare, to abandon any living soldier to the mercy of the Indians. The whole force must be risked to save a single trooper. Yet Custer was to be accused, although not formally, of a repetition of this offense at the Battle of the Washita a little more than a year later. There, it was said, Custer abandoned Major Elliott and a detachment who had been cut off while making a flank attack in obedience to orders.

Whether or not these accusations were true—and there can be no doubt that they were true at least in part—and whether or not, if true, the acts were justifiable, the respect and affection of a considerable proportion of the regiment were alienated. So long as Custer commanded it thereafter, the Seventh Cavalry was not a happy outfit.

And then there were incidents on the march of the regiment to Colorado that were, to say the least, quite unsavory. The Morning Reports of the regiment during this period are evidence of an unhealthy state of discipline in the regiment. There was scarcely a night during which one or more of the troopers did not desert on the trackless plains infested with hostile Indians, armed only with their carbines and a few rounds of ammunition. To desert under such unfavorable conditions one must have impelling reasons.

One afternoon the regiment made camp with several hours of daylight remaining. Without waiting for the protection of night, some ten or twelve troopers "went over the hill." A few took their mounts; others went on foot. Their departure was soon discovered, and some of them were seen in the distance. A specification of one of the court-martial charges against Custer alleged that he ordered the Officer of the Day to pursue the deserters with the guard, and to shoot them down without quarter. The guard set out at once. A few of the deserters were captured and brought back to camp. Two of these had been shot and were seriously, though not critically, wounded. It was further alleged that Custer directed the wounded men to be placed in a wagon, and that he forbade the regimental surgeon to go near them or provide any medical care for them.

The court-martial convicted Custer and sentenced him to loss of rank and pay for one year. Custer served this sentence and rejoined his regiment in 1868; but the reputation of the "boy-general" was tarnished. The effect of this humiliation is apparent during the remaining years of his life. He had been, in his own estimation, the victim of persecution by small jealous competitors. The giant had been stabbed in the back by pygmies. His pride had been severely wounded, and the wound festered, leaving an ugly scar. This scar could be made less noticeable, less disfiguring, only by repolishing his reputation to a brilliance that would blind the public to the defect.

Custer's first effort to re-establish his importance was unsuccessful. His second effort was fatal. His first opportunity came when the scandals of President Grant's administration exploded. Belknap, Grant's Secretary of War, was accused of selling positions, among them the positions of post-trader on Army posts. The post-trader's store was the prototype of the post exchange. It was a private concession, the profits of which often were huge. Custer accepted the invitation of the Senate Investigating Committee to testify against the Secretary of War. Here was his opportunity to have revenge on the "brass hats" in the War Department—and he made all that he could of this opportunity.

But all that he could was not enough. He knew little of his own knowledge. His testimony was mostly hearsay, and would not have been admissible under any rules of evidence. On the one point on which he testified as having personal knowledge he was wrong; and afterward had to retract his testimony. But he had taken advantage of the opportunity to release some of his spleen. This was in March, 1876.

President Grant, never condoning dishonesty nor protecting malefactors, nevertheless was not pleased with this gratuitous attack upon one of his cabinet officers. Especially did he resent such conduct upon the part of an officer of the Regular Army—and more especially because it was apparent that the intent of the attack was merely to smear one of his appointees rather than to offer any acceptable evidence of malfeasance. The

President, however, took no action at the time. But he remembered; and he did not have to remember very long.

In 1868, the United States Government entered into a treaty with the Sioux Nation which guaranteed the Indians a large territory, in what is now the Dakotas, to have and to hold in perpetuity. No white men would be permitted to encroach upon it. This land was not considered valuable to, or particularly usable by, the white man; and there was no reason why the Indian should not have it in exchange for his promise to relinquish all claims to much more valuable lands elsewhere.

But unfortunately it was not known at the time that there was gold in the Black Hills. When this was discovered, the situation was altered. The white man had been "gypped." The fact that he had not known of the presence of the gold when he signed the treaty obviously made the treaty null and void. Any lawyer could prove that.

So, with the discovery of gold, the whites rushed to the Black Hills. The Indians protested this treaty violation to the Government; but the Government was deaf. So the misguided Indians decided to take the matter into their own hands. Any white could have told them that this was a mistake, but the obstinate Sioux were in no mood to listen to reason.

It is not necessary to describe the several tribes of Indians that constituted the Sioux Nation. It is only necessary to point out that there were eight principal tribes in the Nation, and that allied with these were the separate tribes of Cheyennes and Arapahoes. The social organization of the Indian was not sufficiently developed to permit of either large or permanent alliances. So it is a measure of the intensity of the Indians' resentment of this injustice that they were able to perfect an effective alliance of many tribes, and to hold it together for a considerable time.

Two great Indians were largely responsible for the success of the alliance—Sitting Bull, the Hunkpapa medicine man, and Crazy Horse, the Oglala warrior, the greatest tactician ever produced by Indians. Our distorted histories have created the common misimpression that Sitting Bull was the great warrior chieftain of the Sioux. This is not true. He was their great demagogue. But whenever there was any fighting, Sitting Bull repaired promptly to his tepee and occupied himself in making medicine. It is doubtful that his name derived from his posture and his professional incantations, but it is certainly a coincidence.

Active resistance on the part of the Indians commenced in 1875, when they began to commit a series of what, in recent times, are known as overt acts. They roamed beyond the borders of the reservation—their own reservation, within the borders of which the white men were roaming in violation of the treaty. They murdered; they pillaged. They were fighting an undeclared war.

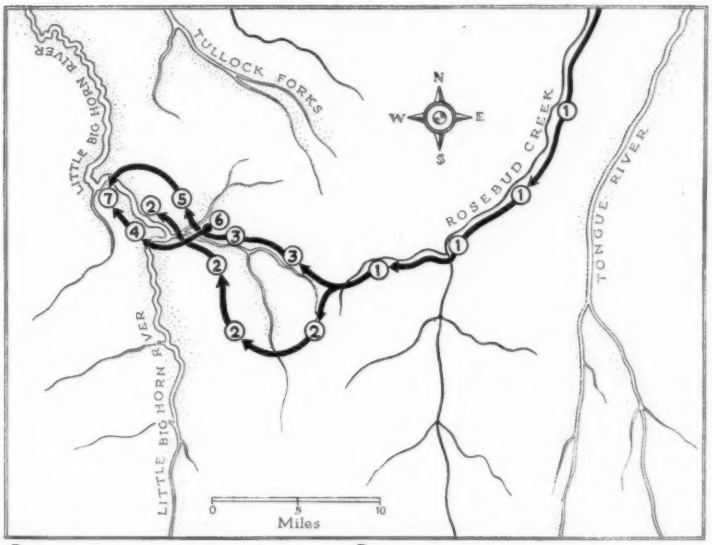
The situation worsened steadily, until in the spring of 1876, the Government decided it could no longer ignore such open rebellion on the part of its wards. An expedition was planned, the purpose of which was to quell the uprising and force the Indians to return to their reservation.

This expedition was planned to consist of three columns of troops: a column under Crook to move northward from Fort Fetterman on the North Platte River (in what is now Converse County, Wyoming); a column under Gibbon to move eastward from Fort Ellis (in what is now Meagher County, Montana); and a column under Custer to move westward from Fort Abraham Lincoln, located just across the Missouri River from Bismarck, North Dakota.

The plan was submitted to President Grant. He approved the plan, but with one important exception: Custer would not be permitted to command any part of the expedition. In fact, he would not even be permitted to accompany his regiment on the expedition. The President had had enough of this publicity hound who thought nothing of embarrassing his Commander-In-Chief in order to promote his own reputation. The chicken of the testimony in the Belknap case had come home to roost.

General Alfred Terry was selected to command both the expedition and the column from Fort Abraham Lincoln. Custer made frantic efforts to be reinstated; but only after the kindly intercession of General Terry did the President relent, and then only in part. Custer could go along in command of his Seventh Cavalry, but he could not command a column—although his rank might entitle him to the command of the eastern column under the over-all command of Terry. Thus Custer's escutcheon was marred by another spot—and such spots were intolerable to George Armstrong Custer. This one, too, must be polished out at the earliest opportunity.

The eastern column left Fort Abraham Lincoln on May 17, 1876. By the 10th of June it had reached the Yellowstone River at a point not far from the location of present Miles City, Montana. Terry had made contact with Gibbon and began to plan the further operations. Crook had not yet been heard from—and was not to be heard from



① Route of march of 7th cavalry
② Benteen's route
③ Route of march of 7th cavalry less Benteen's three troops
④ Reno's route
⑤ Custer's route after Reno's departure
⑥ Dead Warrior Tepee
⑦ Indian village

for some time because Crazy Horse, with a well-armed, well-controlled force was to meet Crook's column on June 17 and treat it so roughly that it had to turn back to camp to lick its wounds.

The location of the Indians had not yet been discovered, and Terry ordered wide reconnaissances of the area. Custer's cavalry searched many square miles during the next week. Some traces of Indians were found, but no Indians. By June 21, Terry had enough information to prepare further plans. Gibbon was to cross the Yellowstone River and march up the Big Horn and Little Horn valleys. Custer was to lead the Seventh Cavalry up the valley of Rosebud Creek to ascertain the direction of an Indian trail which had been previously reported.

Terry's orders to Custer were in writing. They were clear. If this Indian trail led across the divide into the valley of the Little Big Horn, Custer was *not* to follow it, but was to continue on southward for the dual purpose of exploring the area of the headwaters of the Tongue River and of cutting off the escape of any Indians that might be flushed by Gibbon as he marched up the Little Big Horn. After reconnoitering the upper reaches of the Tongue, *and then only*, Custer was to turn westward, cross the divide, and march down the Little Big Horn toward Gibbon. Estimating the time and space factors for both forces, Terry expected Custer and Gibbon to meet in the Little Big Horn valley late on June 26 or early on the 27th.

Custer set off on June 22 with his entire regiment of twelve troops of cavalry—approximately 600 strong—and with some forty friendly Indian scouts. Before they left Terry offered to reinforce the Seventh Cavalry with a Gatling gun battery and four additional troops of cavalry from another regiment. But Custer declined the offer—an action which seems most significant in the light of the subsequent events. Was it that Custer had already decided to do the job alone, not sharing the glory with anyone?

By the evening of the 24th Custer had found the Indian trail he was seeking, and had also learned that it did cross the divide to the valley of the Little Big Horn. His next duty was clear. He should have reported this fact to Terry by courier and continued his reconnaissance to the south. But here was the opportunity to show the world that George Armstrong Custer, assisted only by his own regiment of cavalry, was more than a match for all the Indians on the plains. Why should he share the glory with Terry, Crook and Gibbon? He would show the President, the War Department, and all the people who had persecuted him in the past, just how unjust they had

been—just how greatly they had underestimated him. He would destroy the Sioux alone and unaided. The Lord had delivered them into his hands, and who was he to defy the Lord by passing up this opportunity to reinstate himself as a national hero?

So, at once, during the hours of darkness, the Seventh Cavalry began following the Indian trail leading into the Little Big Horn valley. Custer halted the regiment in the early hours of the morning until his Indian scouts could send him more information. But it was daylight before the Indian camp was located. Custer's previous experience had taught him the inestimable advantage of surprise—to steal upon a camp in the night and deliver a smashing attack in the early dawn before the Indians were even aware of his presence.

Should he now conceal his command during the daylight hours of the 25th, approach stealthily during the night, and deliver his attack at dawn on the 26th? His military judgment said yes. But there was the possibility that Gibbon would have arrived by the morning of the 26th—and sharing this providential opportunity with Gibbon was unthinkable.

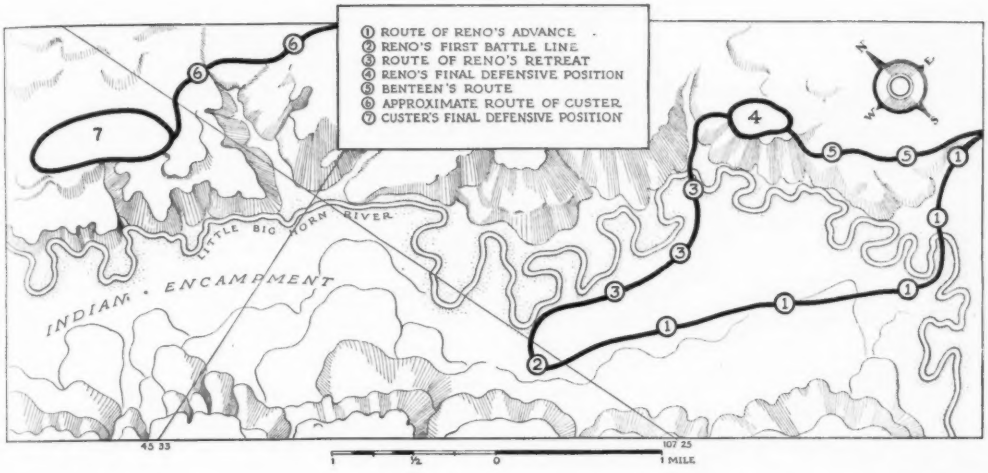
The regiment resumed its march in the daylight. At noon, Custer halted. He ordered Captain Benteen, with three troops, to make a reconnaissance to the left of the direction of march of the main body. The orders given Benteen were vague, and they were further confused by additions and amendments. Benteen afterward testified before a Court of Inquiry that a strict interpretation of his orders would have required him to continue his reconnaissance until stopped by the Pacific Ocean; but, fortunately, Benteen interpreted them reasonably rather than strictly.

Benteen left with his troops, and the main body continued along the Indian trail. Indian signs were fresher, and there were more of them. About 2:00 p.m. the column reached a tepee beside the trail, in which the body of an Indian warrior lay on a bier. Custer never knew it, but this was one of Crazy Horse's braves who had died of wounds on the way back from the fight with Crook. In fact, the trail had been made by Crazy Horse's force.

It was at about this point and this time that the Indian camp became visible in the Little Big Horn valley some five miles distant. Because of the rough terrain intervening, little could be seen of the details of the camp or of the ground over which any attack would have to be made. No further reconnaissance was made, however. With no information as to the strength and disposition of the Indians, and with practically no information as to the terrain, Custer issued orders for the attack. Major Reno was to take three troops and advance rapidly toward the cloud of dust that marked the Indian camp; and, as soon as he came within striking distance, was to charge the camp. Other than telling Reno that his little force would be "supported by the whole outfit," Custer gave him no information of his further intentions. Reno did not inquire, because the relations between him and his commander were strictly official. There were many in the Seventh Cavalry who had never forgiven Custer for abandoning their comrades in previous Indian fights; and the regiment was torn with schisms.

Without further word, Reno set out. He had three miles to go to reach the Little Big Horn River, and this he made at a fast trot. He forded the river about three miles above the Indian camp, and stopped to water his horses. Then he reformed his command in the fringe of trees along the river, and began his advance on the camp. Two of his troops were in the front line with one following closely in reserve—a brave little band of 112 marching on several thousand Indians. After clearing the cover of the trees, they took up the trot. Soon hundreds of Indians were riding to their left, and firing on them from the flank and rear. Already Reno was confronted by many more Indians than his own little command numbered, and he was nowhere near the Indian main body. Reno halted, formed a dismounted battle line and assumed the defensive. He was driven back by hordes of Indians; and, as he fell back, he pivoted on his right flank so as to place the river and the trees on its bank to his rear. The fighting increased in intensity. More and more Indians joined in. The cavalry were losing men rapidly, and it was apparent to Reno that they would all be lost if they continued the attempt to hold this position. He ordered the survivors to mount. The Indians dashed in and fired volleys at point blank range, throwing the troops into confusion. Reno ordered a charge into the mass of Indians. In the confusion, seventeen men were left in the strip of woods; but the rest, led by Reno, literally cut their way through solid masses of Indians and then fled, with horses at a dead run, toward the ford at which they had first crossed the river.

But the Indians kept heavy pressure upon the right of the fleeing column, and it was unable to reach the ford. The troopers were forced across the river about a mile below the ford, and they assembled on a nose of the bluff on the right bank of the river—here to make their last stand which, it seemed evident, would be of short duration.


① ROUTE OF RENO'S ADVANCE
② RENO'S FIRST BATTLE LINE
③ ROUTE OF RENO'S RETREAT
④ RENO'S FINAL DEFENSIVE POSITION
⑤ BENTEEN'S ROUTE
⑥ APPROXIMATE ROUTE OF CUSTER
⑦ CUSTER'S FINAL DEFENSIVE POSITION
LITTLE BIG HORN RIVER
INDIAN ENCAMPMENT
45 33
107 25
1 ½ 0 1 MILE

No sooner had they reached the top of the bluff than they saw a column of cavalry approaching over the high ground. Was this Custer? Was he belatedly coming to their rescue? No, it was Benteen with his three troops. It was a joyful reunion, in spite of the fact that it didn't alter the situation very much. Even with the addition of Benteen's command they were still outnumbered twenty to one by the Indians. It could be only that more of them would perish.

"Where is Custer", they demanded of Benteen. But all Benten knew was that he had been recalled from his reconnaissance mission by a laconic message from Custer, scribbled on a scrap of paper: "Benteen, come on. Big village. Be quick. Bring packs." Upon receiving this, Benteen had turned back until he struck the Indian trail, and had then followed it toward the valley. He had not even waited for the pack train to catch up. Hearing the sound of the firing in Reno's fight, he had cut across the country in its direction. He had supposed it was Custer with the rest of the regiment, who was engaged with the Indians.

Where, then, was Custer? Had he abandoned them as he had abandoned parts of his regiment before? No one doubted that this had happened.

Shortly after Benteen's arrival, other sounds of firing were heard from the direction of the bluffs on the right bank of the Little Big Horn some two or three miles farther down stream. The firing was at first heavy, but gradually lessened and finally ceased. Now the besieged band was certain of what had happened: they decided that Custer had attacked the Indian village, had been repulsed, and had withdrawn, leaving them to their fate. They cursed Custer as they withstood, sometimes with difficulty, the attacks made upon their little stronghold during the late afternoon and evening.

It was a long night. There was much commotion in the Indian village; but eventually this quieted and except for occasional shots fired by Indian snipers, the only sounds were the groans of the wounded and the muttered curses of the embittered soldiers while they waited for their last dawn.

As soon as the hilltops were light, the Indian attack was renewed with vengeance. Reno's little command was completely surrounded, and the Indians were firing on them from all sides. When the Indians crept close enough to make their fire too accurate, the soldiers drove them back with courageous counterattacks.

This bitter fighting continued all morning. If Custer didn't come soon, all would be over. The arrival of the pack train in the late afternoon of the previous day had brought them plenty of ammunition; but their water was exhausted and the sun was terribly hot. A few men, at very great risk, crept to the river to fill their canteens; but these dribbles were only enough for the wounded. The end was in sight.

Suddenly, around noon, the Indians broke off the attack. The soldiers could see the tepees being struck in the Indian camp. Pony herds were collected, and the large force of Indians, with their squaws and children, started slowly westward toward the Big Horn Mountains and gradually disappeared in the distance. That they were mysti-

fied by this sudden tactic of the Indians in no wise lessened the rejoicing of Reno and his men.

Let us return to Custer as he sat on his horse near the "Dead Warrior Tepee," as it became known in history, in the early afternoon of the 25th. He has already dispatched Benteen with three troops on a vague mission. He has just made his decision to attack and has started Reno, with three troops more, on his mission. One troop is some distance to the rear, guarding the pack train that is unable to keep up with the pace Custer set in his impatience to close with the Indians before Gibbon arrives. This leaves Custer only five troops—a total of about 225 officers and men.

He has divided his total force three ways—and this in the face of an enemy of unknown strength on ground that no one in his command has ever seen. It is not a happy situation. Perhaps Custer is not particularly pleased with it. But the urgency of the moment, the overwhelming desire to accomplish this coup without assistance, carries more weight than the evident danger of disaster.

What Custer intended to do with the five troops, which he retained under his own control, can only be surmised. But the circumstantial evidence is rather convincing that he intended to move it down the right bank of the Little Big Horn (instead of crossing the river where Reno crossed) until he was opposite the Indian camp; and there to ford the stream and charge into the village in a direction at a right angle to the direction of Reno's attack—in technical language, an enveloping attack for which Reno should furnish the holding attack, except that the mission given Reno went well beyond the usual scope of a holding attack.

Custer moved to carry out some such a plan. He soon found his column in very rough terrain, in which the high ground near the river was badly cut up by deep gullies, the axes of which were perpendicular to his line of march. This slowed up his march very much; and explains why Reno had been fighting for more than one hour before Custer closed with the enemy.

For another reason, the plan was doomed to failure from the start. Adjacent the Indian camp the right bank of the river was a steep cliff, and the horses could never have reached the stream at this place. But Custer did not know this until too late—if, indeed, he ever knew it. He made no reconnaissance and he knew nothing of the terrain.

As Custer's column was struggling across the narrow gullies in the hills opposite the Indian camp, it was struck without warning by an overwhelming force of savages under Crazy Horse. From the mute evidence left by the bodies of men and horses, there can be no question that this attack had come as a complete surprise. One troop had been completely annihilated in march formation with scarcely a carbine discharged.

The white survivors of this initial assault had formed hasty lines of battle on the top of the ridge opposite the Indian camp. The arrangement of the defense had not been the best in the world; but there had been no time to seek perfection. It would have made little difference. It had all been over in an incredibly short time. There were some carbines here, too, that had not been fired often. Sometimes this was because the trooper didn't live very long. But many other times it was because the brass in the cartridge, made by grafting commercial firms, was of such poor quality that the ejector tore through the lip without removing the spent case. When this happened the soldier had to punch the case out with his ramrod. This slowed his rate of fire, which was slow enough at best because these were only single-shot weapons. The Indians, on the other hand, were armed with the most modern Remington repeating rifles which they had obtained in great numbers in exchange for fur and hides at the trading posts of the American fur companies. That it was a criminal offense to sell, barter or give a firearm to an Indian was no deterrent to these great American merchants.

How shall we evaluate Custer's actions on June 25, 1876, and how shall we account for them? Neither is possible with complete accuracy; but both the evaluation and the explanation of his actions have been subjects of much speculation and many controversies.

As to judgment of his actions, hindsight is always more accurate than foresight. Monday morning quarterbacks are always successful. How much did Custer know when he made his plan of attack? This cannot be answered categorically. Custer was not on social speaking terms with many of his officers, and especially was not with Reno and Benteen who left the main body before Custer discussed its employment—if indeed, he ever discussed it with any of his officers. None in the five troops, that went with him to their doom, had the opportunity of recording any of his further orders. But there is ample evidence that his knowledge of the strength of the Indians was either false or entirely lacking—probably the latter. It is certain that he knew nothing of Crook's defeat.

And no one, with any knowledge of the terrain across the river from the Indian camp, would have selected that area as the place from which to launch an attack. So it is safe to say that Custer knew very little about the situation when he ordered the attack.

This leads only to the conclusion that his action was unsound to the point of recklessness. This was no insignificant campaign against a small band of hostile Indians. The very size of the Army forces indicated that this was generally realized. Terry's instructions urged caution and joint action by the several commands.

Why, then, did Custer pursue this course of action? His defense of his abandonment of parts of his command in previous fights had been that the safety of the bulk of his command demanded such action. Why, on this occasion, did he risk the safety of his command by precipitate action, by attacking in broad daylight at the sacrifice of the important element of surprise, by launching the attack with woefully inadequate information? This, too, is anyone's guess; but motivation by an overwhelming desire to re-establish a reputation that had been sadly damaged by unwise exploits seems to me to be the most satisfactory explanation.

It is a curious chain of events that led to Custer's first difficulties with higher authority which engendered such bitter resentment on his part. How much this resentment governed his future actions may lie in the field of pure speculation, but there is evidence that it did exert a considerable influence. A few cholera vibrio slipped away from Europe with political refugees fleeing persecution. No sooner had their descendants arrived in America than they created havoc along thousands of miles of waterways and other highways of travel. Then, after having retired into obscurity for several years, succeeding generations again migrated, hidden among artisans who were to build an outpost of civilization in the western wilderness, there again to emerge long enough to cause a minor disaster. Finally, after twelve more years of inactivity they crept out once more from hiding to create, in 1867, a situation which exerted a profound influence upon the life and career of George Armstrong Custer.

These generations of microbes traveled thousands of miles. They struck down hundreds of people; but the ultimate tragedy of their making, it seems to me, happened in the valley of the Little Big Horn River almost three decades after they first came ashore in New Orleans.

A PSYCHIATRIST LOOKS AT CUSTER

KARL MENNINGER, M.D., Topeka, Kansas

DR. HAWLEY has asked me as a psychiatrist to make some comments upon the psychiatric implications of his fascinating account. We are given a portion of the case history of a cavalry officer of about 45 who was killed in action. We have the following pertinent data. He was a man:

1. Who stood 34th in his class at West Point.
2. Who was made a Major General at the age of 23.
3. Who achieved a certain amount of military distinction in the services of the Union Army where his actions were characterized by aggressiveness.
4. Who was noted for his ostentatious dressing and bad manners. (See J. C. Haskell and other references cited by Douglas Southall Freeman in *Lee's Lieutenants*, New York, Charles Scribner & Sons, 1944, pages 734 ff).
5. Who at the moment of supreme victory (Appomattox, April 9, 1865) violated military etiquette in many ways, loudly demanding surrender from his defeated and inactive enemy (General Longstreet) while General Lee and General Grant were conferring. (Op. cit.).
6. Who "took care of" and refused to return a famous pair of spurs given by General Santa Ana to the father of one of his friends. (Op. cit.).
7. Who in the name of warfare ordered and executed surprise attacks upon communities of men, women and children and slaughtered the women and children along with the men.
8. Who took his own wife with him to a frontier assignment and later became so worried about her that he was impelled to forget or neglect his military duties.
9. Who deprived wounded soldiers under his own command of medical and surgical attention.
10. Who disregarded the safety and welfare of his troops to the extent of sending them into hostile territory with insufficient military preparation and protection to their almost certain (and quite pointless) death.
11. Who was convicted of one desertion of his own troops and was suspected of others.
12. Who either committed perjury or at least gave incorrect damaging testimony in court to satisfy a personal spite.
13. Who disobeyed specific orders given by the one iriend he seems to have retained and the one General that fntervened in his behalf.
14. Who presumably planned the sacrifice of the lives of the bulk of his command in order to attempt to achieve a minor piece of personal military glory.

From Winter Veterans' Administration Hospital Topeka, Kansas.

These data describe a personality type only too familiar to psychiatrists, falling into a category of psychopathology typically characterized by excessive vanity, complete disregard for the feelings or safety of others, a lack of loyalty either to cause or to friends, either to the principles of humanity or to the established code of ethics, and a conspicuousness of achievement at times passing for success under circumstances where ruthlessness and boldness are to some advantage.

When this type of personality was encountered among the enlisted men in World War II, it was very apt to come rather promptly to the attention of the psychiatrists and such individuals were "boarded out" on Section VIII" or the equivalent. But when a man wears "stars" on his shoulders, he can "get away with" things for which he would be court-martialed or hospitalized were he a private. This is not to imply that this happened often, but every time it happened it destroyed the morale, if not the lives, of thousands of men committed to the charge of such incompetent leaders.

Three corollary questions come to my mind.

First of all, what is to be said of the act of General Terry—a man whose name and reputation are completely unknown to me—who in spite of Custer's bad record, in spite of the court-martial, in spite of bad behavior in connection with the trial of the Secretary of War, and in spite of General Grant's express wishes, insisted on giving a position of leadership and responsibility to a man like Custer?

In the second place, why does the name of Custer still stand in the mind of the average American as that of a great hero?

And thirdly—if by some accident of fate Custer had been successful in his disobedient and ill-planned attempt at coup, what would have been the verdict of history?

REVIEWS OF NEW BOOKS

SINCE the text *La chirurgie en obstetrique*[1] has been prepared for the use of the medical students at the University of Strasbourg, France, it is not particularly detailed in its presentation of the various subjects but strives instead to enunciate principles of surgery as applied to common surgical conditions occurring in obstetrics. The line drawings prepared by the senior author, Dr. Keller, aid greatly in the elucidation of the text.

Surgical treatment of genital abnormalities such as imperforate hymen, acquired sterility due to pelvic inflammatory disease, ectopic pregnancy, appendicitis, stenosed cervix, placenta previa, various types of phlebitis, inversion of the uterus and genital prolapse are a few of the topics discussed. The subjects of immediate repair of perineal tears and of episiotomy are not presented. In view of the audience toward whom this text is directed, this omission would seem to be a definite oversight. A short discussion of genital prolapse is well done.

Many subjects are definitely brought up to date. Ligation of the vena cava, of the utero-ovarian plexus, of the internal iliac and of the common iliac are all mentioned under pelvic thrombophlebitis. Low cervical cesarean section is popular in Strasbourg and is fully discussed. It is given a prominent place in the treatment of placenta previa and of cephalopelvic disproportion.

A plea is made in the preface for unified combined departments of obstetrics and gynecology for teaching, scientific research, and clinical work. Strasbourg and Tarnier are the only such in France. It is stated that those having combined interests are the most observant and the most scientifically productive. Mention is made of the 1921 French Surgical Congress at Paris on Low Cervical Cesarean Section at which Schickele and Brindeau dethroned the classical section and it is further stated that such capacity and understanding presupposes a surgical education preliminary to obstetrical-gynecological specialization. With such training behind him, as Couvelaire says, —"He will not tremble when he holds the scalpel."

VICTOIRE LESPINASSE.

MANY unrelated conditions from various fields of surgery are discussed in *Grandes problemas de clinica quirurgica*.[2] Representative chapters include those on acute appendicitis, hyperthyroidism, cancer of the rectum, fracture of the neck of the femur, Buerger's disease, injuries of the wrist, gastric and duodenal ulcer, and diabetic gangrene. In all, there are thirty-one sections, each devoted to a case presentation followed by a comprehensive discussion of all phases of the problem involved. There is a larger section on infection, presenting the newer knowledge of the mechanisms of infection and immunity, as well as the diagnosis and treatment of infection.

The discussions are interesting, with emphasis clearly placed on the important points, and the material is well organized from a didactic standpoint. The case presentations are careful and complete. There is little that is original, and the volume will be of value chiefly for the teaching of fundamentals.

AURA P. DUKE.

THE small monograph of 208 pages entitled *Introduction to Surgery*[3] by Frantz and Harvey presents in a clear concise manner the fundamental principles of surgery. There are six well arranged sections so grouped that the student may learn and quickly review the essentials he must know.

The instructor of surgery will find the book most helpful if he insists that his students understand its contents. By so doing he can be assured that they have the background necessary to absorb whatever surgical subject he may teach.

As it is true that those who work in surgery should have an understanding of medicine, so too medical men could profit well by reading this book of surgical principles. The authors are to be congratulated upon their excellent and helpful contribution.

RUSSELL T. BOTHE.

THE text on gynecological diagnosis by Professor Neuweiler[4] of Bern combines painstaking thoroughness with strict observance of the limitations imposed by his title. In the first section he describes the proper method of taking the history and carrying out both general and special types of examination. There are excellent illustrations, particularly those of uterosalpingography in a variety of pathological states.

The remainder of the book is devoted to the diagnosis and differential diagnosis of gynecological disease, under headings subdivided according to their anatomical location. Descriptions are accurate and complete and illustrations are abundant.

The text presents the subject almost exclusively from an anatomical point of view. Endocrinological and chemical diagnostic methods are not discussed, nor is functional gynecological disease. The volume should be helpful not only to the student learning practical gynecological diagnosis, but also to the practitioner confronted with the occasional diagnostic problem.

HOWARD ULFELDER.

[1] LA CHIRURGIE EN OBSTETRIQUE. By R. Keller and A. Ginglinger. Paris: Masson et Cie, Editeurs, 1946.

[2] GRANDES PROBLEMAS DE CLINICA QUIRURGICA. By Dr. Alfredo Velasco S. Santiago, Chile: Central de Publicaciones, 1945.

[3] INTRODUCTION TO SURGERY. By Virginia Kneeland Frantz, M.D. and Harold Dortic Harvey, M.D. New York: Oxford University Press, 1946.

[4] LEHRBUCH DER GYNAKOLOGISCHEN DIAGNOSTIK FUER AERETE UND STUDIERENDE. By Dr. W. Neuweiler. Bern: Hans Huber, 1946.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

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PRELIMINARY PROGRAM FOR 1947 CLINICAL CONGRESS NEW YORK, SEPTEMBER 8 TO 12, 1947

THE thirty-third Clinical Congress of the American College of Surgeons will be held in New York at The Waldorf-Astoria from September 8 to 12. Planning of the program is being resumed at the point at which it was discontinued last year when the New York meeting had to be postponed because of the arrangements for the United Nations Assembly. The plans made previously will be carried out for the official meetings, operative and nonoperative clinics, panel discussions, symposia, forums, medical motion picture showings, and technical and scientific exhibits. The twenty-sixth annual Hospital Standardization Conference will also be held as part of the Clinical Congress, with a four-day program of panel discussions, symposia, and round table conferences.

SIXTH NEW YORK CONGRESS

This will be the sixth time that the Clinical Congress has been held in New York. The first time was in 1912, when the old Waldorf-Astoria was the scene of the third Congress. Dr. George E. Brewer was the Chairman and Dr. Charles H. Peck the Secretary of the 1912 Committee on Arrangements. Dr. Edward Martin of Philadelphia was then President of the Clinical Congress of Surgeons of North America. More than 2,600 physicians registered, and the lack of organization for regulating the attendance at the clinics precipitated the proposal by Dr. Franklin H. Martin at the business meeting on November 15, for the creation of the College. Later Congresses were held in New York in 1919, 1924, 1931, and 1938.

CLINICAL PROGRAM

The hospitals and medical schools of Greater New York are co-operating in scheduling operative and nonoperative clinics. The program that they prepared last year under the guidance of the local Committee on Arrangements, when there was prospect of holding the Congress in New York, is substantially the same as that planned for this year, with such revisions as seem desirable in view of scientific developments and changes in personnel. The preliminary program was published in the August, 1946, issue of SURGERY, GYNECOLOGY AND OBSTETRICS, pages 275 to 288.

Visiting surgeons will have ample opportunity to attend well arranged programs of many different kinds in a number of the excellent hospitals in the New York metropolitan area. General and special demonstrations will be held on subjects such as fractures, cancer, maternal morbidity, and end-result studies; newer diagnostic and therapeutic procedures; preoperative and postoperative supportive treatment; anesthesia; and reconditioning. Clinicopathologic and x-ray conferences will also be held. The newer techniques and surgical procedures may be observed.

The medical schools will hold a series of exhibits demonstrating their work, which will be on

display in their affiliated hospitals. The program of each hospital will be arranged to cover subjects in general surgery, obstetrics and gynecology, fractures, orthopedic surgery, thoracic surgery, neurosurgery, genitourinary surgery, and ophthalmology and otolaryngology.

PRESIDENTIAL MEETING

On Monday evening in the Grand Ballroom the Presidential Meeting will be opened with the impressive processional of the officers, Regents, and honorary guests. Welcome to the assembly will be extended by the Chairman of the Committee on Arrangements, Dr. Howard A. Patterson. Dr. Irvin Abell of Louisville, President of the College, will preside and will deliver the Presidential Address. An inaugural ceremony will be held for the incoming officers. Foreign guests will then be introduced.

The second Martin Memorial Lecture will be delivered. This lectureship was established upon motion of the Board of Regents at its midyear meeting on April 1, 1946, as a memorial to both Dr. Franklin H. Martin and Mrs. Martin. The founder of the College and of SURGERY, GYNECOLOGY AND OBSTETRICS was joined by his wife in making the College the beneficiary at their deaths of the Journal, together with its physical plant operated by The Surgical Publishing Company of Chicago, of which they were the owners. Doctor Martin died in 1935 and Mrs. Martin in 1945.

The Martin Memorial Lecture is to be given annually during the Clinical Congress. It will deal with a scientific subject of the author's own choosing. It supplants the former Annual Oration in Surgery.

CONVOCATION

The Convocation is scheduled for Friday evening, the plan of separating it from the Presidential Meeting having proved to be quite successful at the 1946 Clinical Congress in Cleveland. An Assembly of Initiates will be held prior to the Convocation on Friday in order to instruct them in the Convocation procedure and other matters.

The Convocation will open with a processional of officers, Regents, and Governors. The new President, Dr. Arthur W. Allen, will preside and will make the opening remarks, confer the honorary fellowships, and present the candidates for fellowship. Following this ceremony, the Fellowship Address will be given.

SCIENTIFIC SESSIONS

The scientific sessions, to be held on Tuesday, Wednesday, and Thursday evenings, will be addressed by eminent surgeons and specialists, recognized as authorities in their fields. Special scientific meetings will be arranged on the same evenings for specialists in ophthalmology and otolaryngology. The newest developments in general and special fields will be presented in the well rounded program.

Every afternoon, from Monday through Thursday, panel discussions led by recognized authorities in each field, aided by well qualified collaborators, will be held. Similar meetings held during past Congresses have been most successful, largely because they permit the participation of a large number of surgeons, thus increasing the opportunities to learn from the experiences of others.

Preliminary plans include the holding on one afternoon of a symposium on fractures and other traumas, and a symposium on cancer on another afternoon. There is always wide interest in these special meetings. Plans for several new features have been discussed but cannot be announced until definite decisions have been made in cooperation with the Committee on Arrangements.

FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

The Forum on Fundamental Surgical Problems will be conducted on Tuesday, Wednesday, Thursday, and Friday mornings. Included will be brief reports of original clinical and experimental observations relating to the broad aspects of surgery and the surgical specialties. No prepared discussions of the reports are planned, but questions and comments will be invited. Dr. Owen H. Wangensteen of Minneapolis, chairman of the committee which is planning the program, is working toward representation of as many as possible of the various university departments of surgery in this presentation of clinical and experimental research work.

The enlistment of the interest of young men who are doing original work, through the Forum, is one of the most beneficial results of these sessions which are now considered to be an indispensable feature of every Clinical Congress.

HOSPITAL STANDARDIZATION CONFERENCE

The first formal session of the Clinical Congress will be the opening meeting of the twenty-sixth Hospital Standardization Conference. Dr. Irvin Abell of Louisville, President of the College, will preside. The hospital conferences will continue on Monday afternoon, with sessions following on Tuesday, Wednesday, and Thursday mornings, afternoons, and evenings.

Hospital administrators, members of governing boards, heads of the various hospital departments

and their personnel, nursing groups, and many other persons directly or indirectly concerned about hospital progress will be interested in the discussion of current hospital problems. National organizations representing various groups of hospital personnel will co-operate and participate in the meetings, which will include formal sessions, panel discussions, round table conferences, and open forums.

ADVANCE REGISTRATION

The hospitals and medical schools of New York afford accommodations for a large number of visiting surgeons. However, in order to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the meetings and also by accommodations in the hotels. It is therefore expected that surgeons who wish to attend the Congress will register in advance.

The members of the Board of Regents regret that conditions beyond their control will not permit unpaid registration at the 1947 Clinical Congress. They voted to restore the registration fee of $5.00 for Fellows and for endorsed Junior Candidates. Non-Fellows attending as invited guests of the College will pay a fee of $10.00. No fee will be required of initiates of the class of 1947.

To each surgeon who registers in advance a formal receipt will be issued. This is to be exchanged for a general admission card upon his registration at headquarters during the Congress. This card is not transferable and must be presented in order to obtain clinic tickets and admission to scientific sessions.

TECHNICAL AND SCIENTIFIC EXHIBITION

The technical exhibit, together with the registration and clinic ticket bureaus, will be located in the Basildon Room, Jade Room, and Astor Gallery, all on the third floor of the hotel. Leading manufacturers of surgical instruments, x-ray apparatus, sterilizers, operating room lights, ligatures, dressings, hospital apparatus and supplies of all kinds, and pharmaceuticals, and publishers of medical books will be represented in the exhibition.

HOTEL RESERVATIONS

Although the prospect is that the hotel situation in New York will be more favorable than it would have been last year, nevertheless there is still a critical shortage of hotel rooms and early reservations are most desirable. In making these, it is urged that communications be addressed to the New York Convention Bureau, through which all reservations for the Clinical Congress are to clear. No correspondence should be sent directly to the hotels. A letter will be received by all Fellows in which the procedure will be outlined, with which will be enclosed a form to be used in making reservations. First, second, third, fourth, and fifth choices of hotels may be designated. The following hotels are recommended by the Committee:

	Minimum rates with bath	
	Single	Double
Allerton House, 143 East 39th Street	$2.75	$
Allerton House for Women, 130 East 57th Street	3.00	
Ambassador, Park Avenue and 51st Street	6.00	
Astor, Broadway and 44th Street	3.50	4.00
Barbizon (Women), Lexington Avenue and 63rd Street	3.50	
Barclay, 111 East 48th Street	6.00	8.00
Belmont Plaza, Lexington Avenue and 49th Street	4.00	6.00
Beverly, Lexington Avenue and 50th Street	5.00	
Biltmore, Madison Avenue and 43rd Street	5.50	7.50
Bristol, 129 West 48th Street	2.50	3.50
Capitol, 51st Street and 8th Avenue	3.00	4.50
Carlyle, Madison Avenue at 76th Street	6.00	
Chesterfield, 130 West 49th Street	2.50	4.00
Commodore, Lexington Avenue and 42nd Street	3.50	5.50
Concourse Plaza, Grand Concourse and 161st Street	3.50	5.50
Cornish Arms, 311 West 23rd Street	2.25	4.00
Delmonico, 502 Park Avenue	6.00	8.00
Essex House, 160 Central Park South	6.00	8.00
Fifth Avenue Hotel, 24 Fifth Avenue (9th Street)	4.00	6.00
Governor Clinton, 31st Street and 7th Avenue	3.30	4.40
Henry Hudson, 353 West 57th Street	2.50	3.50
Kenmore Hall, 145 East 23rd Street	2.00	3.50
Lexington, 48th Street and Lexington Avenue	4.00	6.00
Luxor Baths Hotel, 121 West 46th Street	2.25	
McAlpin, Broadway and 34th Street	3.30	4.95
Martinique, Broadway at 32nd Street	2.75	3.85
Midston House, 22 East 38th Street	3.50	4.00
New Weston, Madison Avenue and 50th Street	4.00	7.00
New Yorker, 34th Street and 8th Avenue	3.85	5.50
Paramount, 46th Street, West of Broadway	3.00	5.00
Park Central, 7th Avenue and 55th Street	4.00	6.00
Parkside, 18 Gramercy Park South	2.75	
Pennsylvania, 7th Avenue and 33rd Street	3.85	5.50
Piccadilly, 227 West 45th Street	3.00	5.00
Plymouth, 143 West 49th Street	2.50	3.50
President, 234 West 48th Street	2.50	4.00
Prince George, 14 East 28th Street	2.50	4.00
Roosevelt, Madison Avenue and 45th Street	4.50	6.50
Shelton, 49th Street and Lexington Avenue	3.50	5.00
Taft, 7th Avenue and 50th Street	3.00	5.00
Times Square, 43rd Street and 8th Avenue	2.25	4.00
Tudor, 304 East 42nd Street	2.50	
Victoria, 7th Avenue and 51st Street	3.00	4.50
Waldorf-Astoria, 50th Street and Park Avenue	7.00	
Warwick, 54th Street at Sixth Avenue	5.00	
Wellington, 7th Avenue and 55th Street	3.00	4.50
Woodstock, 127 West 43rd Street	3.00	5.00

CLINICAL CONGRESS PROGRAM IN BRIEF

Monday

9:30 General Assembly for Surgeons and Hospital Representatives, Grand Ballroom
1:30–3:00 Panel Discussion, Empire Room
2:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
2:00 Hospital Conference, Sert Room
2:00 Surgical Film Exhibition (General), Grand Ballroom
3:30–5:00 Panel Discussion, Empire Room
8:15 Presidential Meeting, Grand Ballroom

Tuesday

8:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
9:00–12:30 Forum on Fundamental Surgical Problems, Grand Ballroom
9:30 Hospital Conference, Sert Room
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Jensen Suite
10:00 Surgical Film Exhibition (General), Empire Room
11:00 Panel Discussions
Ophthalmology—Otorhinolaryngology
1:30–3:00 Panel Discussion, Grand Ballroom
2:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals.
2:00 Hospital Conference, Sert Room
2:00 Symposium on Fractures and Other Traumas,
2:00 Surgical Film Exhibition (General), Empire Room
3:30–5:00 Panel Discussion, Grand Ballroom
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
7:30 Hospital Conference—Trustees, Sert Room
8:00 Scientific Session, General Surgery, Grand Ballroom
8:00 Scientific Session, Ophthalmology, Jensen Suite
8:00 Scientific Session, Otorhinolaryngology, Le Perroquet Suite

Wednesday

8:00 Meeting of Cancer Committee, Carpenter Foyer and Dining Room
8:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
9:00–12:30 Forum on Fundamental Surgical Problems, Grand Ballroom
9:30 Hospital Conference, Sert Room
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
10:00 Surgical Film Exhibition (General)
State and Provincial Committees:
9:30 Executive Committees
10:15 Credentials Committees and Committees on Applicants
} Empire Room
11:00 Judiciary Committees
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
12:00 Meeting of Board of Governors, Jensen Suite
1:30–3:00 Panel Discussion, Grand Ballroom
2:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
2:00 Symposium on Cancer, Empire Room
2:00 Surgical Film Exhibition (General)
2:00 Hospital Conference, Sert Room
3:30–5:00 Panel Discussion, Grand Ballroom
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
7:30 Hospital Conference, Sert Room
8:00 Scientific Session, General Surgery, Grand Ballroom
8:00 Scientific Session (Eye, Ear, Nose and Throat), Empire Room

Thursday

8:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
9:00–12:30 Forum on Fundamental Surgical Problems, Grand Ballroom
9:30 Hospital Conference, Sert Room
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
10:00 Surgical Film Exhibition (General), Empire Room
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
1:30 Adjourned Meeting, Governors, Grand Ballroom
1:45 Annual Meeting, Fellows, Grand Ballroom
2:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
2:00 Hospital Conference, Sert Room
3:00 Panel Discussion—Graduate Training in Surgery, Jensen Suite
3:30–5:00 Panel Discussion, Grand Ballroom
3:30 Surgical Film Exhibition (General), Empire Room
3:30 National and Regional Fracture Committee, Le Perroquet Suite
4:00 Committee on the Library, Room 4-J
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
8:00 Scientific Session, General Surgery, Grand Ballroom
8:00 Scientific Session, Ophthalmology, Empire Room
8:00 Scientific Session, Otorhinolaryngology, Sert Room

Friday

8:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
9:00–12:30 Forum on Fundamental Surgical Problems, Grand Ballroom
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
10:00 Surgical Film Exhibition (General), Empire Room
1:30 Assembly of Initiates, Grand Ballroom
1:30 Panel Discussion, General Surgery
2:00 Clinics, Demonstrations and Clinical Group Conferences, selected local hospitals
2:00–4:00 Panel Discussions
Obstetrics, Sert Room
Plastic Surgery, 4-U Blue Room
Neurological Surgery, Assembly Room M-N
Thoracic Surgery, Jensen Suite
Urology, Le Perroquet Suite
Orthopedic Surgery, Carpenter Foyer and Dining Room
2:00 Surgical Film Exhibition (General), Empire Room
3:30 Panel Discussion, General Surgery
8:15 Convocation, Grand Ballroom

BOARD OF REGENTS OF AMERICAN COLLEGE OF SURGEONS CONSIDERS DELAYS IN APPOINTMENTS TO HOSPITAL STAFFS

COMPLAINTS having come from several sources about difficulties being placed in the way of returning medical veterans who were applying for hospital privileges, the Board of Regents of the American College of Surgeons at a meeting in Hot Springs, Virginia, on April 24, carefully considered the problem of helping veterans and other younger surgeons in obtaining appointments. Several specific cases of seemingly unjustifiable delay were studied, together with such contributory hospital conditions as the existing shortage of beds and long waiting lists of patients. The result of the deliberation was the presentation and adoption by the Board of Regents of the following resolution:

WHEREAS it has come to the attention of the American College of Surgeons that many well trained surgeons, especially returned veterans, who have located or have signified their intention of locating in communities where there are hospital facilities, have been denied hospital privileges until they had been in residence in that locality for six months to a year.

BE IT RESOLVED that the Board of Regents of the American College of Surgeons disapproves of the practice, and although fully cognizant of the shortage of hospital beds, the Board believes that such well trained, competent, and ethical individuals should be given similar opportunities as offered established medical practitioners of the community.